BUREAU OF HYGIENE AND TROPICAL DISEASES.

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LEPROSY.

MUIR (Ernest). **The Control of Leprosy. The Charles Franklin Craig Lecture of the American Society of Tropical Medicine.**—*Amer. Jl. Trop. Med.* 1937. Jan. Vol. 17. No. 1. pp. 51–58.

This lecture summarizes very well the present position of the leprosy problem. Compulsory segregation is condemned as leading to the easy concealment of patients, the diagnosis in whom may sometimes be difficult in any case. Much has been learnt from surveys, which revealed the real number of cases in India to be up to ten times as many as the obvious ones recognized by non-medical census enumerators. Although the value of treatment has sometimes been exaggerated it is certainly more effective in leprosy than in tubercle, and its chief value is in gaining the confidence of the patients and rendering their follow-up and the tracing of contacts easy, and thus greatly simplifying its control through education of the people in simple measures of household and village isolation of the infective cases, which are not more than one-fourth of the whole number. The decline of leprosy in England in the Middle Ages is attributed largely to the segregation of patients in the 250 leper hospitals then existing. In West Africa, Muir found the native chiefs recognized leprosy readily, but had completely wrong ideas regarding infectivity; for they look on the crippled nerve cases as the most, and the nodular type as the least, dangerous. Here education again is essential for control measures. They also thought it safe for children to mix with lepers, as they did not recognize their infection in childhood with development of the disease mainly during adolescence. The success of segregation in Norway was due to a wisely planned campaign in a civilized country with a well developed health service, so a carefully planned programme in accordance with social conditions is essential in each leprous country. The propaganda-treatment-survey plan has proved successful in India. In Nigeria, with 200,000 cases, or 1 per cent. of the population, leper villages are of value in addition to the more costly settlements. In the Philippines clinics and local leprosaria have wisely been provided. Improvement of hygienic conditions is of great importance, but necessarily a slow process in backward poor areas. A good diet with sufficient vitamins is also of value. The use of these measures may in time open the door towards public health and social reform. *L. Rogers.*

Lowe (John). **The Epidemiology of Leprosy.**—*Indian Med. Gaz.* 1937. Mar. Vol. 72. No. 3. pp. 160–166. With 2 maps & 4 graphs.

This general account of the subject is in close agreement with current opinion. In a brief historical survey, based largely on the book of Rogers and Muir, the author found no satisfactory explanation of the decline of leprosy in Europe. Transmission is through direct contact with infectious cases, due, he thinks, most probably to insects. Maps are given of the rough general distribution in hot damp climates of the world, and that of India based on recent surveys with a very similar relationship to climate. He is also in agreement with others regarding age and sex distribution, the excess in males being difficult to explain. The predisposing effects of poor diet and social conditions are stressed. The most important point in control is the prevention of contact of children with infectious cases. *L. R.*

Flandin (Ch.) & Ragu (Jean). Origine, mode de contagion, durée d'incubation de la lèpre dans 95 cas dont 6 contractés dans la région parisienne. Traitement par les injections intraveineuses du complexe chaulmoogra-cholestérol. [**Leprosy: Its Source, Mode of Infection and Length of Incubation Period. Treatment by Intravenous Injection of Chaulmoogra and Cholesterol.**]—*Bull. Acad. Méd.* 1937. Mar. 16. 101st Year. 3rd Ser. Vol. 117. No. 11. pp. 337–343.

This is an instructive study of 26 leprosy patients in the Saint-Louis Hospital and 69 more in Paris and its neighbourhood. The great majority were infected in French Colonies, including 22 natives, 9 half-castes, 17 whites born in, and 41 who had visited, leprosy infected colonies, and only 6 whites who had never left France. Details regarding the conditions under which the last six contracted the disease show that two of them had lived in close contact with Chinese and Annamites in Paris, and of the remaining four, three contracted the infection through cohabiting with an infective leper woman; and the fourth was a young girl who had married a white leper, with periods of only six to eight months of sexual contact before signs of the disease were observed. He concludes that under ordinary social conditions in France the danger of contracting leprosy is too slight to necessitate segregation measures and compulsory notification. He had previously reported good results from treatment with a combination of chaulmoogra and cholesterol, which removes infectivity and is attracting cases to come for treatment who would only hide themselves under a compulsory isolation system. *L. R.*

Fabre (Maurice). Léproserie de Valbonne. [**The Valbonne Leprosarium.**]—*Rev. d'Hyg. et de Méd. Préventive.* 1936. Dec. Vol. 58. No. 10. pp. 758–764. With 2 figs.

This is a brief general account of a small isolated leprosarium founded to accommodate some of the lepers from the Paris Hôpital Saint-Louis.

L. R.

CLOUSTON (T. M.). **Age Groups of Leper Patients at Nauru.**—*Leprosy Review.* 1937. Jan. Vol. 8. No. 1. pp. 23–29.

The complete control of the small population of Nauru Island during the serious outbreak of leprosy makes the data of great importance. In this note 284 isolated bacteriologically positive cases and 193 early negative ones treated as out-patients are analysed as regards age and sex. In the later years the number of new positive cases has greatly decreased, but negative early ones not to the same extent. This is attributed largely to the segregation of the infective cases at the earliest possible moment, due to frequent examinations of all the small population for the first symptoms [as advocated for the island by the reviewer over a decade ago] having removed a source of infection, especially for the children. The fewer cases now reaching the infectious stage is considered to point strongly to the advisability of early and continued treatment, for only four originally non-infectious cases have gone on to nodular formation under treatment, and in the last six years, five have become infectious skin cases, but not nodular ones. Further, only 17, or 6 per cent., of early infectious cases on admission have advanced to the nodular stage under treatment, but 32 cases at some time nodular have been released after becoming bacteriologically negative, or approximately 11 per cent., and 12 more cases have lost their nodules.

The sex incidence shows a ratio of 1·2 males to 1·0 females admitted to segregation, and of 1·41 females to 1·0 males in clinic cases. The relapse rate has been only 8·8 per cent. readmitted to segregation, less than elsewhere, and 8 of 9 recent ones gave negative leprolin tests by Muir's technique, indicating a lowered resistance. In nerve cases in the clinic the relapse rate appears to be very low, and to the ease with which regular and prolonged treatment can be carried out on this small island this good result is attributed.

As regards age, approximately 55 per cent. of the segregated cases could have been infected before the age of 15 years and about 45 per cent. were definitely infected before that age. At least 20 per cent. were over 25 on the first signs appearing, and 15 per cent. over that age when first exposed to infection.

The present situation on the island shows only 57 segregated and 102 clinic cases, or a total of 159 under treatment, approximately 10 per cent. of the population. This "contrasts very favourably with the figure of almost 30 per cent. in 1924 and 14 per cent. at the end of 1933." *L. R.*

BECHELLI (Luiz Marino). Contagio conjugal na lepra. [**Leprosy from Conjugal Association.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1936. Vol. 4. Numero especial. pp. 349–354. [10 refs.]

From a study of 506 cases in which one of the married couple was a leper the author has traced infection to the partner in 49, or 9·7 per cent. Further, infection by conjugal contact nearly always occurred, as one would expect, in the earlier years of cohabitation. That the infection is not more often acquired is ascribed by the author to lessened receptivity in adult life, or to the possibility that frequently repeated contagion leads to the development of a certain degree of immunity. *H. H. S.*

Wilson (R. M.). **Marriage among Lepers.**—*Internat. Jl. Leprosy.* Manila. 1936. Oct.–Dec. Vol. 4. No. 4. pp. 441–443.

The author reports further favourable results from allowing recovered lepers to marry after sterilizing the males, but allowing them to adopt one child from the colony. Three years' experience finds the eleven families happy and well. On the other hand, of seventeen couples who married without permission, or sterilization of the men, within about a year nine children were born, but no more after the men were promptly vasectomized. Meanwhile four mothers relapsed under the strain of pregnancy and lactation, and no orphanages have been found to take the babies. *L. R.*

British Empire Leprosy Relief Association. **Leprosy : a Problem of Colonial Development. Report for 1936.**—32 pp. With 11 figs. London : 131 Baker Street, W.1.

This report deals with the work carried out in African and many other British Possessions other than India, which the Indian Council report covers. It includes brief accounts of Dr. Muir's West African tour already dealt with in reviews of *Leprosy Review*, and the Leprosy Exhibition of the Association which visits various towns and arouses much interest. The work of the Toc H volunteers, mainly in West Africa, is also favourably reported on. *L. R.*

Leprosy Review. 1937. Jan. Vol. 8. No. 1. pp. 1–50. With 7 figs. (1 map) on 4 plates.—Quarterly Publication of the British Empire Leprosy Relief Association, 131 Baker Street, London, W.1. [1*s.* 6*d.*]

The number commences with a leper survey of the Arabian Peninsula by W. H. Storm, who reports that although a few cases can be found in any area, it is only in the southern end of the peninsula in Yemen and Wadi Ooan and in Ohufar that definite foci of infection have been found. Yemen cases are to be met with in the Aden Protectorate.

A lecture by H. C. de Souza-Araujo on Leprosy in Brazil covers ground dealt with by him in previous years. He has submitted a plan for the national control of the disease to the Government. The article on Leprosy in Ceylon by R. G. Cochrane also deals with work already published.

C. M. Hasselmann records a case, illustrated by a photo and a microscopical section, of adenoma sebaceum et acanthoides cysticum, which might easily be mistaken for an advanced case of nodular leprosy of the face until the microscope reveals an enormous increase in the sebaceous glands with adenomatous and cystic changes.

A report of the Sudan Medical Service for 1935 shows a total of 10,711 lepers including an estimated excess of 2,250 over the known cases. 4,210 are under treatment and 4,251 under observation. Camps and settlements contain 390 segregated and 2,308 additional ones under treatment. New settlements are being formed and voluntary settlements near dispensaries were to be opened in 1936. It is reported the percentage that had been rendered quiescent has risen from 31 per cent. in 1932 to 78 per cent. in 1935, but the stage has been reached in which further chaulmoogra treatment is of no avail in cases under observation prior to 1933–34. Few advanced cutaneous and mixed cases respond to treatment. Methylene blue

has proved disappointing in advanced cases. Less than 10 per cent. of the cases are considered to be a danger to their neighbours. "Treatment is effective and worth trying in a large percentage of active early cases over a period not exceeding four years. The settlements have removed the chief foci of infection in the district, and both centralized and simplified their control."

The Public Health Report of S. Rhodesia for 1935 records that 1,311 cases were treated in two large government settlements and 48 more in a small mission one, and the admissions in that year numbered 249. The total cared for has risen from 508 in 1929 to 1,359 in 1935, mostly volunteers. The settlements are looked on as curative hospitals and 319 were discharged last year as "arrested" cases.

In Nyasaland the annual report showed 213 admissions, 131 discharged and 47 deaths. Queensland had 63 segregated patients at the end of 1934.

An important paper on leprosy in Nauru Island is dealt with separately. *L. R.*

Leprosy Review. 1937. Apr. Vol. 8. No. 2. pp. 51–100. With 9 figs. on 2 plates. Quarterly Publication of the British Empire Leprosy Relief Association, 131 Baker Street, London, W.1. [1*s.* 6*d.*]

This number includes a paper on the diagnostic value of gland puncture by H. v. R. Mostert based on 80 cases that had been classed as maculo-anaesthetic leprosy with palpable glands. A few drops of saline were injected into a gland, withdrawn again after massaging the gland and stained with Ziehl-Neelsen method. In 13 cases positive results were obtained and on re-examining these patients 8 showed very early nodular infiltration of the face, and 6 of them also erythematous rash on the body and other parts. The remaining 5 positive cases also showed a similar rash or active macular lesions, and subsequent scrapings of the skin of the face proved to be positive. Thus the gland punctures served as a guide to the diagnosis of early cases of nodular retrogression.

The organization of occupational therapy at the Dichpali leper home and hospital is described by George M. Kerr. 170 of the 700 patients are being educated, and the remainder were divided into gangs for various forms of domestic and agricultural work, including a malarial gang, who all worked three hours a day. Only a small part of the food supply is yet grown by the men, but it is increasing. The patients realize the benefit to their health from such occupation.

A short description of the India Purulia leper home is contributed by E. Muir. It includes an independent village occupied by the healthy descendants of former leper inmates as a standing evidence against the old hereditary theory of leprosy.

H. P. Lie contributes a short account of the work of his famous compatriot worker at leprosy, Dr. Danielssen, and an obituary notice of Mr. Wellesley Bailey, the founder of the Mission to Lepers, is also of interest. *L. R.*

Vlach (Giuseppe). Un caso autoctono di lebbra a Trieste.—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1937. Mar. Vol. 18. No. 3. pp. 175–186. With 12 figs.

MEDULLA (Candido). L'odierna nosografia della lebbra in Cirenaica.—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1937. Mar. Vol. 18. No. 3. pp. 163–174. With 2 figs.

BECHELLI (Luiz Marino). O tempo de incubação da lepra. [**The Incubation Period of Leprosy.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1936. Vol. 4. Numero especial. pp. 355–360.

The author investigated 529 cases but was able to obtain reliable information in 273 only. The average incubation in these was 8·4 years. In 101 it ranged between 6 and 10 years; the minimum was 2 years and the maximum 28. He maintains, therefore, that examination of contacts should be repeated up to 10 years after exposure to possible infection. *H. H. S.*

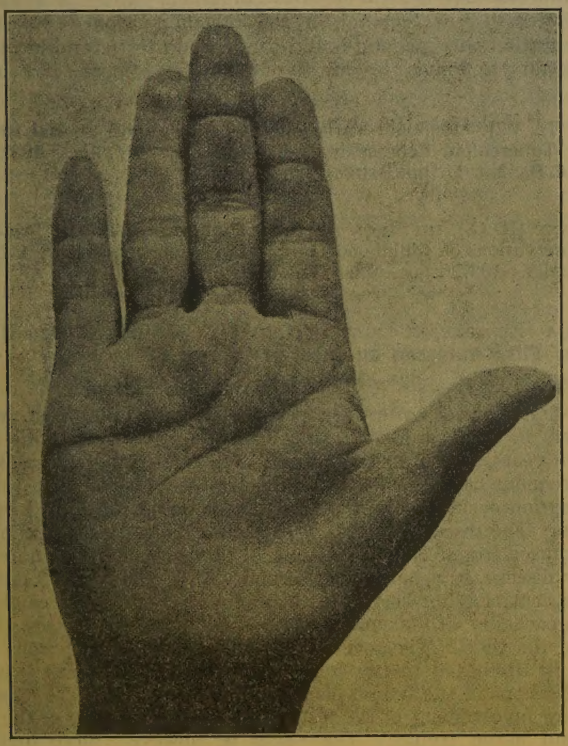
WADE (H. W.). **The Skin Lesions of Neural Leprosy. I. General Introduction. II. Observations in Cebu.**—*Internat. Jl. Leprosy.* Manila. 1936. Oct.–Dec. Vol. 4. No. 4. pp. 409–430. With 1 fig. [22 refs.]; 1937. Jan.–Mar. Vol. 5. No. 1. pp. 1–30. With 36 figs. on 6 plates.

These papers are detailed descriptions of the pathological changes in the skin in nerve leprosy which should be read in original by those interested. The first of them deals with the material studied, terminology and classification, activity or quiescence of the lesions, technique and the nature of the histological changes in a general manner.

In the second paper the grouping of the lesions in 52 cases is discussed in detail, and the appearances of the skin lesions illustrated by excellent photos of early cases; the primary object "being to determine the essential pathology of the lesser forms of the non-lepromatous lesions of leprosy." Clinically the lesions examined varied from the slightest possible to active major tuberculoid leprides, and it was found that the simpler active leprides are always tuberculoid in some degree. Quiescent lesions retrogressed from active ones also showed slight tuberculoid changes in five of eight cases, but of thirteen residual lesions only three showed tuberculoid foci, and two specimens from nonmacular anaesthetic patches were practically negative. The papulate minor tuberculoid leprides are as a class retrogressive. Three of four diffuse minor tuberculoid lesions showed the usual changes, as did three major ones. "The findings as a whole indicate strongly the constancy of tuberculoid changes in all typical active leprides of whatever clinical variety." *L. R.*

CAMPOS (Nelson de Souza) & LONGO (Paulino W.). Atrophia circunscripta aos musculos da eminencia thenar como manifestação inicial e residual da lepra. [**Atrophy of the Thenar Muscles in Leprosy.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1937. Mar. Vol. 5. No. 1. pp. 29–51. With 10 figs. English summary.

The authors have observed and here record five cases of localized wasting of the muscles of the thenar eminence in leprosy. It may come on early, within 2 months of symptoms making their appearance. By carefully carried out electrical reaction tests they found that the terminal motor branches of the ulnar nerve were involved, these going



Showing atrophy of muscles of the thenar eminence in early leprosy.
[Reproduced from *Revista Brasileira de Leprologia.*]

to the flexor brevis, adductor pollicis and the first dorsal interosseous. [The ulnar, it will be remembered, innervates only the median head of the flexor brevis pollicis, the lateral being supplied by a branch of the median nerve.] *H. H. S.*

SCHUJMAN (Salomon). **Tuberculoid Lepra Reaction.**—*Internat. Jl. Leprosy.* Manila. 1937. Jan.–Mar. Vol. 5. No. 1. pp. 77–86. With 18 figs. on 4 plates.

This article has been translated from the *Revista Argentina de Dermatosifilogia* **19** (1935), 411–435, and is illustrated by naked eye and histological appearances. The author has met with seven cases of reactions in tuberculoid leprosy and made bacteriological and histological examinations in five. In three the reactions occurred spontaneously, in one after injections of aniline drugs, and in three after chaulmoogra treatment. The general condition of the patients remained good with no fever, but disturbances of sensibility were marked, and infiltration appeared in the lesions, although they and the

nasal mucosa were usually negative bacteriologically. A frank tuberculoid structure was found in the reacting lesions. Erythrocyte sedimentation was moderate, and the leprolin tests frankly positive; the contrary to nodular lesions, so of diagnostic import. *L. R.*

WADE (H. W.). Regional Variations of Leprosy with Special Reference to Tuberculoid Leprosy in India.—*Leprosy in India.* 1937. Jan. Vol. 9. No. 1. pp. 3–13. [22 refs.]

COCHRANE (R. G.), DE SIMON (D. S.) & FERNANDO (A. C.). Preliminary Observations on Childhood Leprosy in Ceylon.—*Internat. Jl. Leprosy.* Manila. 1937. Jan.–Mar. Vol. 5. No. 1. pp. 61–65.

MITSUDA (Kensuke) & OGAWA (Masako). **A Study of One Hundred and Fifty Autopsies on Cases of Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1937. Jan.–Mar. Vol. 5. No. 1. pp. 53–60.

The first named writer has performed over 1,000 post-mortems on lepers in the last forty years, and 150 have been done in the last five years, and are summarized. As usual, tuberculosis was the most frequent cause of death with a rate of 54·7 per cent., and the complication occurred oftenest in cutaneous cases weakened by lepra reaction. The disease is usually less acute than in other people, but it has caused from 52 to 55 per cent. of the total deaths in nine years. Kidney disease, as usual, comes second with a total of 13·3 per cent., 4·7 per cent. having been due to uraemia. Septicemia caused 9·8, leprous cachexia 4·0, laryngeal stenosis 1·3 and other causes 17·3 per cent. of the total. The severity of ulcerations and affections of the larynx is attributed to the cold climate. The cutaneous type only showed lesions in the lymph glands and viscera, but nerve cases may also show involvement of the testes and more frequently of the spinal cord and nerve trunks. The vagus is, however, more frequently attacked in cutaneous cases, as are the bones. Tuberculous changes on the viscera are the result of generalization and have no relation to tuberculoid skin changes. *L. R.*

CERRUTI (Humberto). Os bacillos de Hansen nos tecidos: aspecto interessante na fixação pelo formol. [**Hansen's Bacillus in the Tissues.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1936. Dec. Vol. 4. No. 4. pp. 441–446. English summary (10 lines).

This paper is of interest to those engaged in studying the morbid histology of leprosy. Tissues are usually fixed in one or other of the following fluids: alcohol, 70 per cent.; formol, 10 per cent. in neutralized physiological saline; Zenker, or formol-Zenker (Helly's fluid); Orth-Müller, or Bouin. However good for fixing tissues where the histological changes are to be studied, none of the last four is satisfactory where demonstration of the bacilli is aimed at. For this purpose either of the first two is good in maintaining the alcohol-acid fast properties of the organism. Where vascular organs such as liver or spleen are under investigation, most of the bacilli appear very dark brown or black if formol is used for fixation, particularly if the tissues are placed in the fixing fluid within a short time of death.

H. H. S.

MITSUDA (Kensuke). **The Significance of the Vacuole in the Virchow Lepra Cells, and the Distribution of Lepra Cells in Certain Organs.**—*Internat. Jl. Leprosy.* Manila. 1936. Oct.–Dec. Vol. 4. No. 4. pp. 491–508. With 8 figs. on 2 plates.

The author has studied the distribution of lepra cells, with special reference to lipoid degeneration revealed by staining with Sudan III, in lymph nodes, liver and spleen and other organs. He came to the conclusion that the leprosy bacillus invades the histiocytes, causing them to multiply and form vacuolar nodules. In the organs, except the testicles, it does not form tumour-like masses as in the skin, but only small nodules in the liver, spleen and glands and in the suprarenals. He considers that the production in the tissues of lipoid substances and vacuoles is peculiar to leprosy, and that chaulmoogra preparations accelerate the production of lipoid and the natural degeneration of the bacilli in the cells. *L. R.*

ERMAKÓVA (Nína). **Studies on Leprosy. II. Formation, Distribution and Diagnostic Significance of Pigment.**—*Internat. Jl. Leprosy.* Manila. 1936. Oct.–Dec. Vol. 4. No. 4. pp. 445–454. With 4 figs. on 1 plate.

The author reports finding an iron-containing pigment in the affected tissues of old leprosy cases, in large quantity in nodular, but very little in maculo-neural and tuberculoid, which he thinks is of local origin. A considerable degree of phagocytosis was constant. Its presence in tuberculoid leprosy may serve to distinguish such lesions from true tubercle due to Koch's bacillus. The pigment is in the form of haemosiderin. *L. R.*

MUNEUCHI (Toshio). **On the Leprous Changes of the Endocrine Organs.**—*Kitasato Arch. Experim. Med.* 1937. Jan. Vol. 14. No. 1. pp. 61–74. With 12 figs. (2 coloured) on 6 plates.

This well illustrated paper can best be summarized in the author's own conclusions.

" Pathological examination of various endocrine glands of 190 autopsied cases of leprosy revealed more or less leprous changes in all the glands. It was only nodular cases which showed lepra cell infiltrations in the glands. In nerve leprosy lepra cell infiltration was seen only in testes and the change was mild and rare. Among the endocrine glands the testes showed the most marked leprous changes. In a nodular case the specific leprotic changes were always noticed, even macroscopically. Adrenal glands also showed almost always small leprous nodules macroscopically. The pineal bodies and ovaries showed fairly marked changes microscopically, but it was usually difficult to notice them by naked eye. The changes in pancreas, thyroid and parathyroid glands were comparatively mild. The changes in the pituitary bodies were the slightest." *L. R.*

MCKNIGHT (Robert S.) & LINDEGREN (Carl C.). **Bactericidal Effects of Vapors from Crushed Garlic on** *Mycobacterium leprae.*—*Proc. Soc. Experim. Biol. & Med.* 1936. Dec. Vol. 35. No. 3. pp. 477–479.

The following " strains of acid-fast and non acid-fast Mycobacterium leprae " were used in these experiments. A non acid-fast yellow strain

obtained from Dr. Beckwith, a non acid-fast orange strain from Dr. Kessel and an acid-fast yellow strain from the American Type Culture Collection. Petri dish agar cultures were spread with a heavy suspension of the organisms and one gram of garlic placed on the inverted cover so as not to be in contact with the cultures, and incubated for three days, together with controls without the garlic after exposing the plates to the garlic vapours for from one minute to two hours. They found that after 32 minutes the growth was markedly inhibited and after an hour or more practically no growth occurred.

L. R.

HAGEMANN (Paul). Fluoreszenzmikroskopischer Nachweis von Leprabakterien im Nasenschleim und im Blut. [**Fluorescence of Lepra Bacilli.**]—*Deut. Med. Woch.* 1937. Mar. 26. Vol. 63. No. 13. pp. 514–518. With 1 fig.

This is a technical paper describing an apparatus for demonstrating fluorescence of lepra bacilli. *L. R.*

KEDROWSKY (W. J.). Variabilité du groupe d'actino-mycètes et son rapport à la doctrine de la nature mycèlienne des virus de la tuberculose et de la lèpre.—*Giorn. di Batteriol. e Immunol,.* 1936. Sept. Vol. 17. No. 3. pp. 289–323. With 4 figs. [20 refs.]

VAN BREUSEGHEM (R.) & MOULES (E.). Pratique de la coloration du bacille de Hansen dans les frottis. [**Staining Hansen's Bacillus.**]—*Ann. Soc. Belge de Méd. Trop.* 1937. Mar. 31. Vol. 17. No. 1. pp. 137–139.

The authors report that they found the following the simplest and best method of staining lepra bacilli in tissues for the use of their native laboratory assistants. Stain with ordinary Ziehl heated for two to three minutes, or cold for two hours. Decolourize with 1 part of nitric or sulphuric acid to 9 parts of 95 per cent. alcohol, and re-stain for 30 seconds with Kuhne's blue. *L. R.*

EDDY (Bernice E.). **Attempted Cultivation of** *Mycobacterium leprae.*—*Internat. Jl. Leprosy.* Manila. 1937. Jan.–Mar. Vol. 5. No. 1. pp. 31–43. [18 refs.]

The author records negative results from the use of 68 culture media enumerated in his paper. The bacilli may persist for long but no evidence of their multiplication could be obtained. *L. R.*

DUBOIS (A.), GAVRILOV (W.) & VAN BREUSEGHEM (R.). Injection intradermique de bacilles de Kedrovski chez le lépreux et le non-lépreux. [**Intradermic Injections of Kedrowski's Bacillus.**]—*Ann. Soc. Belge de Méd. Trop.* 1936. Dec. 31. Vol. 16. No. 4. pp. 483–486.

The researches of MITSUDA, confirmed by others, show that the intradermic injection of killed lepra bacilli of Hansen and of rat leprosy bacilli of Stephansky give reactions in patients with nerve leprosy with few bacilli and in recovered cases, but not in active cutaneous cases containing numerous bacilli. The authors tried similar tests

with Kedrowski's bacillus but obtained different results in leprosy cases. They therefore agree with HAYASHI and MUIR that Kedrowski's organism is not closely related to that of leprosy. *L. R.*

MENDES (Ernesto) & GRIECO (Vicente). Interpretação da reacção leprotica suas relações com a parallergia. [**Parallergy and the Leprotic Reaction.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1936. Vol. 4. Numero especial. pp. 1–25. [17 refs.] English summary.

The lepra reaction is often explained by sensibilization of an allergic subject by the specific agent, *Myco. leprae, i.e.*, by allergy. On the other hand it is by no means infrequently seen in those with mixed or tuberculous leprosy where the organisms may be relatively few, and it may occur apart from definite incitement by the organism, for example, intercurrent disease, physiological disturbance such as onset of menstruation, appendicitis, dental sepsis and so forth. To this condition—reaction of a person in a state of allergy to non-specific agents, protein or otherwise, but differing from the specific antigen producing the allergy—the authors (with MORO and KELLER) apply the term " parallergy." *H. H. S.*

ISHIBASHI (Takeo). Beiträge zur Serologie der Lepra, mit besonderer Berücksichtigung der für die Komplementbindungsreaktion bei Lepra wirksamen Antigene. Nebst serologischen Untersuchungen an Seren von mit säurefesten Bazillen immunisierten Kaninchen. [**Complement Deviation and other Serological Tests in Leprosy.**] —*Tohoku Jl. Experim. Med.* 1937. Jan. 30. Vol. 30. Nos. 3 & 4. pp. 287–314. [10 refs.]

The author reports on elaborate investigations of the complement deviations with antigens prepared from various acid-fast bacilli from those of the different varieties of tubercle to smegma bacilli, and also on agglutination reactions with the sera of rabbits immunized against such antigens. The following are the most important results obtained. The Wassermann reaction by Kolmer's method in 138 cases of leprosy was positive in 22·5 per cent., varying from 39·7 per cent. in nodular cases to 3·7 per cent. in nerve ones. A saline emulsion of ether soluble fractions of acid-fast bacilli gave positive reactions in 90·9 per cent. of nodular and 83·7 per cent. of nerve cases. With an antigen made from the avian tubercle bacillus positive reactions were obtained in 78·9 to 91·1 per cent., so he regards this antigen as of diagnostic value. Agglutination reactions with the sera of his immunized rabbits were positive in dilutions of from 320 to 1,280 with different preparations. *L. R.*

PIMENTEL IMBERT (M. F.). **Rubino's Reaction in Leprosy.**—*Puerto Rico Jl. of Public Health & Trop. Med.* 1936. Dec. Vol. 12. No. 2. pp. 257–266. With 2 figs. on 1 plate. [10 refs.] [Spanish version pp. 246–256.]

This is a good account of the history and present position of the Rubino test. The author has used Rubino's latest method with a

double series of three tubes, each containing respectively increasing dilutions of serum, fresh blood formalinized corpuscles, and non-formalinized corpuscles to serve as a control, with the following results :—

" We tested Rubino's reaction in 278 sera : 47 from lepers, 214 from cases suffering from other conditions, and 17 from apparently normal individuals.

" The agglutino-sedimentation of sheep's red blood cells formalinised (or Rubino's reaction in its latest form) gave us a percentage of 70·21 per cent. positive reactions in all cases of leprosy studied by us.

" The nodular form of leprosy gave a percentage of 86·21 positive reactions ; mixed leprosy, 70 per cent. ; nerve leprosy, 62·4 per cent. There was no reaction in non-leprous cases." *L. R.*

Lamborn (W. A.). **The Haematophagous Fly** *Musca sorbens*, **Wied., in Relation to the Transmission of Leprosy.**—*Jl. Trop. Med. & Hyg.* 1937. Feb. 15. Vol. 40. No. 4. pp. 37–42. [15 refs.]

The author records further work on the rôle of insects in transmitting the infection of leprosy, which he believes to be very important. He quotes previous work indicating that *M. domestica* may carry lepra bacilli from open cases to infect other skin lesions, but thinks non-biting blood-drinking flies require further investigation in this connexion. He has therefore worked with *M. sorbens* in Nyasaland, which prefers to feed on blood serum or pus of open sores or mucous membranes, including leprous ones. He has found lepra-like bacilli in their excreta after a feed on leprous ulcers, which may thus be carried to ordinary sores, cuts or abrasions, or the mucous membrane at orifices such as the nose, which these flies affect. *L. R.*

Costa (Henrique de Moura). As doses fortes de chaulmoogra no tratamento da lepra. [**Large Doses of Chaulmoogra in the Treatment of Leprosy.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1937. Mar. Vol. 5. No. 1. pp. 67–86. English summary.

The author's findings and observations are based on 62 patients only, 44 adults and 18 children. His results are presented mostly in the form of protocols, giving the stage of disease, the time of treatment, the amount of the drug used and the results, whether improved or stationary, and the continued presence or diminution or absence of bacilli. He tested also the effects of the larger doses on the rate of corpuscle sedimentation. For the details given in the many tables the original must be consulted. His method of procedure and the results may be summed up as follows :—

For adults, if the usual dose was 5 cc. weekly, he gave 10 or even 15 cc. two or three times in the week, and for children 0·6–0·9 cc. per kilo. per week in place of 0·2–0·3 cc. This treatment was maintained in some cases for two years, the tolerance being good. There were no instances of toxic symptoms, nearly all patients increased in weight, and their blood sedimentation rate was increased, and clinically the improvement was much more marked than with the smaller doses and especially in children. *H. H. S.*

i. Mercken (G.). Essai de traitement de la lèpre par injections intraveineuses de bleu de méthylène. [**Methylene Blue Intravenously in Treatment of Leprosy.**]—*Ann. Soc. Belge de Méd. Trop.* 1936. Dec. 31. Vol. 16. No. 4. pp. 493–501. With 1 fig.

ii. Occhino (A.) & Kernkamp (Y.). Le bleu de méthylène dans le traitement de la lèpre. [**Methylene Blue in Treatment of Leprosy.**]—*Ibid.* pp. 503–506.

i. The author reports amelioration of nerve symptoms and pain for a time following this treatment up to a maximum of three months, but no effect on the general evolution of the disease. He treated 34 cases.

ii. These workers treated 22 cases and noted after doses exceeding 30 cgm. violent and depressing, but not dangerous, reactions, while the therapeutic value of the treatment was absolutely nil. *L. R.*

Braga (Renato). Tratamento das ulceras leproticas por injecções intrarteriaes. [**Treatment of Leprotic Ulcers by Intra-arterial Injection.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1936. Dec. Vol. 4. No. 4. pp. 447–467. With 11 figs.

The treatment adopted, arterial injection of 1 per cent. methylene blue in quantities of 5–10 cc. at weekly intervals, has given good results in the author's hands. The technique is no more difficult than intravenous injection, and he has so far employed the method in ulceration of the legs. He gives details of seven patients and illustrations of five. [Intra-arterial injection of mercurochrome 220 and of methylene blue for septic conditions is not new ; it was employed more than two years ago by Goinard, Mondzain-Lemaire and Pietri and by Valerio, but the reviewer has seen no previous record of its use in leprosy.]

H. H. S.

Montel (R.), Montel (G.) & Nguyen Ngoc Nhuan. Essais de traitement de la lèpre par la phénol-sulfone-phtaléine. [**Trials of Phenol-Sulphone-Phthalein.**]—*Bull. Soc. Path. Exot.* 1936. Dec. 9. Vol. 29. No. 10. pp. 1064–1067.

This dye is given intravenously every two or three days in 5, 10 and 15 cc. doses of 0·006 gram per cc. up to a total of 185 cc. in 26 days in one patient and 173 cc. in 35 days in another. The urine remained free from albumen. The leprous lesions became stained of a red colour and improved rapidly, so although it is too early to report the ultimate results the method is considered to be worthy of further trial.

L. R.

Montel (R.), Montel (G.) & Le Van Phung. Essais de traitement de la lèpre par la cystéine en injections intraveineuses. [**Trial of Cystein Intravenously.**]—*Bull. Soc. Path. Exot.* 1936. Dec. 9. Vol. 29. No. 10. pp. 1061–1063.

In this note the authors report on four cases of leprosy treated first by methylene blue with improvement in three, but when they ceased to progress he gave intravenous injections of 0·5 gram cystein three times a week up to 20 injections. The patient who had proved

resistant to methylene blue also failed to respond to cystein, but the other three showed considerable further improvement, so it is believed to be a useful adjuvant treatment. *L. R.*

COCHRANE (R. G.) & RAJ (M. Paul). **Alcohol Injections for the Relief of Nerve Pain in Leprosy.**—*Leprosy in India.* 1937. Jan. Vol. 9. No. 1. pp. 18–19.

This is a brief report on two cases of nerve leprosy in which 5 minims of 80 per cent. alcohol were injected into thickened ulnar nerves. In one with an oedematous nerve immediate relief of severe pain was obtained, with no recurrence up to six weeks. In the other only a few hours relief was afforded. It is important to avoid injecting the drug into the subcutaneous tissues as it is extremely painful. *L. R.*

TISSEUIL (J.). Essai de traitement de lèpres cutanées par le sérum sanguin de lèpres nerveuses. [**Nerve Leprosy Serum in Cutaneous Leprosy.**]—*Bull. Soc. Path. Exot.* 1937. Mar. 10. Vol. 30. No. 3. pp. 227–230.

In view of the frequency with which nerve cases of leprosy are free from cutaneous symptoms and the reverse, the author has tried separating the serum from blood taken from a pure stationary nerve case, heating it at 54–56°C. for an hour on three consecutive days, and injecting from 10 to 20 cc. subcutaneously at 3 to 7 day intervals up to a total of 170 cc. in five cutaneous cases of leprosy. No check on the evolution of the disease was noted, but only some amelioration of the general condition. *L. R.*

VAN BREUSEGHEM (R.). Essais thérapeutiques dans la lèpre. I. Le calcium. II. Le carbone intraveineux. [**Calcium Treatment.**] —*Ann. Soc. Belge de Méd. Trop.* 1936. Dec. 31. Vol. 16. No. 4. pp. 537–547.

I. Calcium chloride intravenously has been reported to have been of benefit in leprosy by KLINGMÜLLER and others. The author has therefore tried it, but without obtaining any amelioration of the condition of the patients in eleven maculo-nerve cases even when given with chaulmoogra oil preparations, but in some the lepra reactions were quickly extinguished.

II. He has also tried injecting intravenously 2 per cent. suspensions of animal charcoal with negative results. *L. R.*

ROTBERG (A.). Tratamento da reacção leprotica pelo carvão por via endovenosa. [**Treatment of the Leprotic Reaction by Charcoal Intravenously.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1936. Vol. 4. Numero especial. pp. 163–173. [10 refs.] English summary.

This procedure has been recommended and the author has tried it in 25 patients and four of these a second time. Of the 25 three had

the nervous form, fourteen the mixed, five the maculo-anaesthetic and three the nodular. The charcoal was given in 50 μ particles suspended in 2 per cent. saline, 5 cc. being injected every other day, in the first series of 21 cases. Four remained unaffected, two were made worse, fifteen improved, but the amelioration was not maintained, relapses occurred in some soon after the treatment was stopped, in others actually while the treatment was being carried on. Rise of temperature, headaches and drowsiness were common. In a second series of eight, 4 of the former and 4 new, 5 μ particles were used in 2 per cent. suspension in 10 per cent. dextrose. Tolerance was better, but not the results; 4 were unchanged, 4 improved, 2 relapsed. The author concludes that the method has little to recommend it. *H. H. S.*

Cole (Howard Irving) & Cardoso (Humberto). **Purification and Esterification of Chaulmoogra Oils.**—*Internat. Jl. Leprosy.* Manila. 1936. Oct.–Dec. Vol. 4. No. 4. pp. 455-468. With 2 figs.

This is a technical paper describing the apparatus and method of purifying chaulmoogra oils. The authors find that the time of esterification is not a reliable criterion for determining the completion of the reaction, but refractive index readings should always be used. The influence of sulphuric acid and other factors on the rate of esterification is described, and a method taking approximately eight hours, and the apparatus used, are described. Methods for the preparation of creosoted and iodized esters are given in detail, for which the original paper must be consulted by those interested. *L. R.*

Pereira (Loiola). On the Effects of Alepol on Leprosy.—Reprinted from *Antiseptic.* 1936. July. 3 pp.

Saliba (Nagib). A physiotherapia no tratamento moderno da lepra, Cryotherapia. [**Cryotherapy in the Treatment of Leprosy.**]—*Brasil-Medico.* 1937. Feb. 13. Vol. 51. No. 7. pp. 281-286. With 8 figs. [26 refs.]

The value of carbolic acid snow in the treatment of leprosy is extolled as the best method, being easy to carry out and not violent in its action. Observations are made on eight patients and photographs reproduced to show the conditions of some of them. Paldrock is quoted as saying that the snow modifies the leprosy in such a way that the body is rendered capable of eliminating it. The three chief agents in dermatological practice (not for leprosy only) are X-rays, radium and CO_2-snow. *H. H. S.*

Lagoudaky (Socrates). **Self-Inoculation of Leprosy—Second Communication.**—*Jl. Trop. Med. & Hyg.* 1937. Apr. 1. Vol. 40. No. 7. pp. 77–79.

In this paper the author records the effects of further treatment of his infection with fairly satisfactory results. He chose antilepra intravenously, an " ester-like " derivative of chaulmoogric acid, which was

also taken orally in tablet form. By the end of January 1935 he had received 69 tablets, 24 intravenous and 18 intramuscular injections, with remarkable results in causing some lepromata on his hands to clear up as well as macules. Further similar treatment, however, left a stationary condition, and the intramuscular injections became very painful. Later, further improvement occurred and various lesions disappeared by March 1936 after taking 658 tablets and having 25 intravenous injections until his veins became blocked, and 73 intramuscular ones. His general health remained good two years after his inoculation. His medical adviser recommends further intensive treatment. *L. R.*

MALARIA.

Hicks (E. P.) & Majid (S. Abdul). **A Study of the Epidemiology of Malaria in a Punjab District.**—*Records of the Malaria Survey of India.* 1937. Mar. Vol. 7. No. 1. pp. 1–46. With 11 charts (1 folding). [20 refs.]

The Karnal District in which these observations were made is in the Punjab plain, which has been subject in the past to fulminant epidemics of malaria. Six villages in this district have been kept under almost continuous observation for eight years. The main object of the investigation was the measurement of the factors, infection and immunity, in an area subject to epidemic malaria.

The average enlarged spleen was found to be the best measurement of immunity, its size increasing steadily and consistently in those children who are more immune ; it is, moreover, but little affected by changes in the dose of infection from season to season and from year to year. The measurement of the dose of infection is the product of the crescent rate and the mean catch of *A. culicifacies*. This, unfortunately, does not give full weight to the influence of climate on the longevity of the mosquito. The fluctuations in the dose of infection are sufficient to explain fluctuations in the incidence of malaria. There was little evidence of fluctuations in the immunity of the population in the period under review. When the level of infection is raised for a single year the increase in immunity is small. The authors conclude that fluctuations in malaria in Karnal are almost entirely due to fluctuations in the dose of infection which is determined, chiefly, by the length of the period of low saturation deficiency. This period depends more on an even distribution of rain than on the total rainfall. This résumé does but scant justice to a paper that should be consulted in the original by those interested. *Norman White.*

Field (J. W.). **A Case of Severe Subtertian Malaria with Recovery.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1937. Apr. 19. Vol. 30. No. 6. pp. 565–568. With 2 coloured figs. on 1 plate.

In view of the paucity of published information regarding the highest degree of infestation with malaria parasites compatible with life, considerable interest attaches to the case of subtertian malaria described in this note. The patient, a male Tamil aged 30, was being treated with intramuscular injections of atebrin musonate. On the fourth day thin blood films were examined and gave the following results : Red blood cells counted, 5,000 ; parasites 896 ; infected cells 797 ; single infection of cells 682 ; double infection of cells 93 ; triple infection of cells 8 ; quadruple infection of cell 1. There were large numbers of segmenting parasites. The total parasite count was in the neighbourhood of 660,000 per cmm. The patient recovered.

N. W.

Field (J. W.) & Niven (J. C.). **A Note on Prognosis in Relation to Parasite Counts in Acute Subtertian Malaria.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1937. Apr. 19. Vol. 30. No. 6. pp. 569–574.

This is an interesting attempt on the part of the Malaria Research Division of the Institute for Medical Research, Federated Malay

States, to give statistical precision to the belief that prognosis in acute subtertian malaria bears some relationship to the number of parasites in the peripheral blood. A study was made of 750 cases on admission to hospital, none of whom had had recent malaria treatment. Most of the cases were adult males, Chinese, Indian or Malay. The following table, produced from the report, gives details of the parasite counts :—

Death Rate in Relation to the Parasite Count on the First Day of Treatment in 750 Cases of Acute Subtertian Malaria.

	Trophozoite Counts per cmm. of Blood on 1st Day of Treatment.					
	Under 5,000	5,000 to 25,000	25,000 to 100,000	100,000 to 250,000	250,000 to 500,000	Over 500,000
Cases	209	261	205	57	10	8
Deaths ...	1	0	1	4	2	5
Death rate per cent. ...	0·5	0	0·5	7	20	63

There were only two deaths among 675 cases with counts of less than 100,000 per cmm. Among 75 cases with counts above 100,000 there were eleven deaths. Counts made after the administration of malaria drugs are a less reliable indication of severity, though providing useful information of progress. The extreme limit of tolerance of Asiatic adults for the local strains of *P. falciparum* is probably in the region of 750,000 parasites per cmm. of peripheral blood. *N. W.*

Friedmann (J.). Zur Frage der Beziehungen zwischen Epilepsie und Malaria. [**Relationship between Epilepsy and Malaria.**]—*Wien. Klin. Woch.* 1937. Apr. 30. Vol. 50. No. 17. pp. 565–567. [26 refs.]

This paper is written in honour of the 80th birthday of Wagner-Jauregg.

A case is described of a person who went through the war from 1914 to 1918. After the war he went to Albania as an electrical engineer from 1920 to 1928. There he had " heat stroke," and fell and injured his head. He was unconscious for half an hour. Shortly after he had an attack of fever and malignant tertian parasites were found in the blood. He had relapses in spite of treatment by quinine. About this time he had epileptic seizures. He stated the seizures were of two kinds ; severe, lasting 1½ to 3 hours, there was no warning, the tongue was bitten ; slighter, which lasted a very short time and were announced by a feeling of faintness, discomfort and shivering. His doctor stated that the attacks of epilepsy were connected with the malarial attacks. The author thinks that the " heat stroke " in Albania may have been cerebral malaria. He discusses the *pros* and *cons* of malarial encephalitis being responsible for the epileptic attacks. He concludes by saying that of all diseases epilepsy has the most features in common with malaria. As is well known in malaria there is a definite periodicity,

in epilepsy there is an unrecognized rhythm, the cause of which is completely unknown. As regards the treatment of developed cases of epilepsy by malaria-therapy further study of certain kinds of cases is required. *E. D. W. Greig.*

Pieri (J.), Bouet, Flori & Aubanel. Leucémie lymphoïde et paludisme. [**Leukaemia and Malaria.**]—*Marseille-Méd.* 1936. Dec. 25. Vol. 73. No. 36. pp. 719–723.

This is a description of a case of leukaemia in a man aged 57 who had suffered from chronic malaria. There was a fairly general glandular enlargement. The red blood cells numbered 4,600,000 and the white cells 590,000, an unusually high leucocytosis. Of the white cells no less than 96 per cent. were mononuclear, the remaining 4 per cent. being polynuclears. No large mononuclears were noted. He was submitted to radio-therapy with benefit to his general condition. On his discharge from hospital red cells numbered 5,420,000, white cells 4,000, of which 74 per cent. were mononuclears. The author raises the question as to whether the frequently repeated attacks of malaria from which the patient suffered during twenty years may not have been the cause of this form of leukaemia [designated by the author, Touraine's Splenocytoleukaemia, differing from the ordinary lymphocytic leukaemia]. *N. W.*

Rduch (Hugo). Beitrag zur Frage der Kriegsmalaria. Ein Fall von febris Bang. [**War Malaria. A Case of Undulant Fever (Abortus Type).**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1937. Apr. Vol. 41. No. 4. pp. 379–380. With 1 fig. [Summary appears also in *Bulletin of Hygiene.*]

Patient had suffered from malaria from 1908–1911 and from 1916–1918. In 1918 he had blackwater fever in Palestine. In 1934 he had attacks of fever. To November 1935 he was treated for malaria; then he came under the care of the author. No parasites were found in his blood and the spleen was not enlarged. However, he was given a course of atebrin and plasmoquine, but without effect on the fever. Then the blood was tested for agglutination with the Bang's bacillus and was found to agglutinate the latter up to 1 : 2,000. He was then treated with a Bang vaccine (Behring) and made a good recovery. This then was an example of a fever erroneously attributed to "war malaria" and treated as such. *E. D. W. Greig.*

Jerace (Felice). La splenomegalia malarica nei bambini curata con il metodo di Maurizio Ascoli. (Nota preventiva.) [**Splenomegaly in Malaria treated by Ascoli's Method.**]—*Policlinico.* Sez. Prat. 1936. Aug. 31. Vol. 43. No. 35. pp. 1562, 1565.

Ascoli in 1930 advocated the treatment of splenomegaly in chronic malaria by the intravenous injection of a solution of adrenalin in small doses of from 1/100 to 1/10 mgm. Very successful results have been reported, to confirm which the author treated three children, aged 4, 6 and 9 years respectively, from the Agro Romano, all of whom were suffering from chronic malaria, having been infected and reinfected since infancy. The initial doses were 1/100 mgm. in one

case and 1/200 mgm. in the others. After 15 injections, the final dose being 1/20 mgm., a reduction of 6½ cm. in the size of the spleen was noted in one case and of 4 cm. in another. In the case of a malignant tertian infection a febrile attack occurred on the third day of treatment, with parasites in the peripheral blood, probably the result of treatment; a three days' treatment with quinine 0·60 gm. a day was interposed. The results of treatment were uniformly satisfactory; there was no sign of intolerance and the children were able to follow their normal occupations during treatment. Not only was there a rapid reduction in the volume of the spleen but also a noteworthy improvement in the blood, the leucocyte formula returning to normal.

N. W.

DE NEGRI (Ugo). Cura della splenomegalia malarica secondo Maurizio Ascoli. Ia nota. [**Treatment of Splenomegaly by Ascoli's Method.**] —*Policlinico.* Sez. Prat. 1936. Nov. 30. Vol. 43. No. 48. pp. 2158–2159.

This is a record of seven patients, ages varying from 15 to 50, suffering from chronic malaria with very large spleens, and treated by the intravenous injection of adrenalin. Injections were given once a day, starting with a dose of 1/100 mgm. which was increased gradually to 1/10 mgm., the maximum dose. The treatment was continued for from 30 to 40 days. The results were good; in all cases there was a marked reduction in the size of the spleen. *N. W.*

ASCOLI (M.), MISSIROLI (A.), BONFIGLI (A.), CASU (A.), DILIBERTO (U.), MUSUMECI (N.), RIOLO (P.), ROCCA & TERENZIO. Relazione su di un esperimento compiuto nell' Agro Pontino sulla cura di Maurizio Ascoli nella infezione malarica. [**Ascoli's Treatment of Malarial Infections.**]—*Policlinico.* Sez. Prat. 1937. Apr. 5. Vol. 44. No. 14. pp. 559–62, 665–6, 669–70. With 16 figs.

CANOVA (Francesco). Trattamento della splenomegalia malarica. [**Treatment of Malarial Splenomegaly.**]—*Ibid.* pp. 670–672. [12 refs.]

The report of Ascoli and his colleagues gives full clinical details of 17 men, 17 women and 6 children, all suffering from chronic malaria with enlargement of the spleen, who were treated by Ascoli's method of intravenous injections of adrenalin. No ill effects from the treatment are reported. The results were very satisfactory. Rapid improvement of the patients' condition, cessation of splenic pain, noteworthy improvement of the blood, reduction more or less marked in the size of the spleen, increase in weight and restitution of the capacity to work were marked results of the treatment.

Canova reports the results of treatment, in Transjordania, of 19 cases of chronic malaria by Ascoli's method. The usual doses of adrenalin were used, from 1/100 to 1/10 mgm. The author speaks highly of the value of the method. He further treated 24 cases of acute malaria with adrenalin in association with quinine. Adrenalin is said to counteract the depressive action of quinine, to stimulate the circulation and to lessen the risk of relapse by liberating parasites that have taken refuge in the spleen. *N. W.*

Canova (Francesco). Associazione chinino-adrenalinica nel trattamento della malaria acuta.—*Riv. di Malariologia.* Sez. I. 1937. Vol. 16. No. 1. pp. 31–33. English summary (8 lines).

Ascoli (M.). Tatsachen und Fragestellungen meiner neuen Malariatherapie. [**Facts and Problems of my New Malaria Therapy.**]—*Muench. Med. Woch.* 1937. Mar. 5. Vol. 84. No. 10. pp. 370–371. With 2 figs. [27 refs.]

The author's treatment consists in the intravenous injection of adrenalin, the scheme of dosage recommended is as follows: begin with 1/100 mgm., give daily increasing doses, 1/90, 1/80 up to 1/10 mgm. The last dose is repeated daily for 20 days. In cases of marked malarial splenomegaly it may be advisable to increase the dose provided the drug is well tolerated. Cicchitto, who treated 135 cases of malaria in Italian East Africa, recorded that adrenalin administration reduced considerably the period of treatment of acute cases of malaria and also the quantity of quinine required for a cure. As regards the effect on relapses after treatment his pupil, Riolo, noted that in 15 out of 18 cases of chronic malaria treated two years previously, and a further 20 cases treated one year previously the reduction in the size of the spleen was maintained and there was no relapse. He considers that adrenalin by reducing the congested portions of the enlarged spleen destroys the breeding ground of the malaria parasite. *E. D. W. Greig.*

Mangiacapra (Armando). L'opoterapia splenica nella malaria. [**Treatment of Malaria with Spleen Extract.**]—*Riv. di Malariologia.* Sez. I. 1936. Vol. 15. No. 6. pp. 428–440. [12 refs.]

A summary of the conclusions at which the author has arrived regarding the value of spleen extract in the treatment of malaria. During six years no less than 610 cases have been so treated. Spleen extract has no direct action on the malaria parasite and none on the fever. It has therefore no therapeutic value in acute malaria or in the early stages of chronic malaria. In older chronic infections it can be used with marked benefit. It increases organic immunity, stimulates the reticulo-endothelial system and phagocytosis, improves the blood condition and general nutrition, and effects a marked reduction in the size of the spleen. It is thus a valuable adjuvant in the treatment of chronic malaria. It has, moreover, a slight power of reactivating latent infections. *N. W.*

Farinaud (J.). La prophylaxie du paludisme par les médicaments synthétiques en Indochine, ses conditions et ses possibilités. (Note préliminaire.) [**Synthetic Drugs in the Prevention of Malaria.**]—*Bull. Soc. Path. Exot.* 1936. Dec. 9. Vol. 29. No. 10. pp. 1085–1090.

In spite of the admitted efficacy of the synthetic remedies in controlling malaria incidence, their prophylactic use is of limited applicability in Indo-China, where malaria can be considered as hyperendemic for not less than nine months of the year. *N. W.*

Clark (H. C.) & Komp (W. H. W.). **A Sixth Year's Report on Malaria in Panama (Chagres Valley) with Reference to Drug Control.**—*Amer. Jl. Trop. Med.* 1937. Jan. Vol. 17. No. 1. pp. 59–77.

Previous reports by the authors on drug control of malaria in Panama have been noted in this *Bulletin* (1936, Vol. 33, p. 835; 1935, Vol. 32, pp. 434, 784). The object of the study is to find a suitable compromise in malaria control that can be used by business organizations in the tropics to increase labour efficiency in places where satisfactory antimosquito measures are not possible. The year under report was a period of low malaria incidence following the epidemic period of 1935, thus corroborating the authors' views regarding the cyclic nature of malaria incidence in Panama. As before, monthly blood-parasite surveys in three groups of villages were carried out. In one group blood-positives were treated under supervision with atebrin-plasmoquine; in the second group blood-positives were treated under supervision with quinine-plasmoquine. In the third control group blood-positives received quinine if they desired it; there was no supervision. The average monthly parasite rates in the three groups were 9·1, 12·3 and 18·5 per cent. respectively. Of those examined in every one of the twelve monthly surveys, 59·9 per cent. had parasites in their blood at some period of the year. A high parasite rate can exist at all ages of a relatively tolerant population. Adequate treatment lowers the parasite rate during an inter-epidemic period. Relapses, especially during a year of low incidence, are responsible for a great part of the malaria observed. Infected adults, even though relatively tolerant to malaria infection, will not be able to support the strain of daily hard labour without medical attention. Non-medical personnel in the field, to give immediate antimalaria treatment to those who become clinically ill, supervised by a qualified physician making weekly visits of inspection, should suffice.

N. W.

Robin (L. A.). Conceptions ancienne et moderne du traitement et de la prophylaxie chimique du paludisme. (Application à l'élément militaire dans les zones endémiques.) [**Old and New Conceptions of the Curative and Prophylactic Drug Treatment of Malaria, with Special Reference to the Protection of Troops in Endemic Areas.**]—*Rev. Service Santé Milit.* 1937. Feb. Vol. 106. No. 2. pp. 151–176. [22 refs.]

A well-written and interesting account of the changed outlook on drug therapy and prophylaxis of malaria that has evolved during the last twenty years. Though there is nothing new or revolutionary in the author's ideas his well controlled observations on the relative value of quinine and the synthetic drugs in labour forces in south Indo-China are of interest. In hyperendemic areas prophylactic quinine rigorously administered is often insufficient to maintain the efficiency of a military force. If the force is mobile, however, and camp can be moved every three weeks and pitched not nearer than two thousand metres from native villages and at a distance from frequented roads and paths, the prophylactic administration of drugs can maintain the efficiency of the force even in hyperendemic areas.

N. W.

Jolly (A.) & Sicault. Nouveaux cas d'évolution complète du *Plasmodium praecox* dans le sang circulant. [**Complete Development of *P. praecox* in the Circulating Blood.**]—*Bull. Soc. Path. Exot.* 1936. Apr. 1. Vol. 29. No. 4. pp. 389–390.

In three cases of malignant tertian malaria from Morocco the blood films showed all stages of development of the parasites up to mature schizonts and crescents. The proportions of the various stages were not the same in the three cases. *C. M. Wenyon.*

Lourie (E. M.) **Studies on Chemotherapy in Bird Malaria. IV.—Failure to promote Drug-Resistance in *Plasmodium cathemerium* by Prolonged Administration of Quinine or Plasmochin.**—*Ann. Trop. Med. & Parasit.* 1935. Dec. 18. Vol. 29. No. 4. pp. 421–433.

An attempt was made to produce drug-resistant strains of bird malarial parasites (*P. cathemerium*) by administering to infected birds in series daily doses of quinine hydrochloride or plasmoquine. At no time in the series of bird passages did it appear that the virulence of the parasites was affected or that they were acquiring drug resistance. The claim of previous workers to have produced such strains is critically examined, the conclusion being reached that the evidence they have advanced is inconclusive. *C. M. W.*

Huff (Clay G.) & Bloom (William). **A Malarial Parasite infecting all Blood and Blood-forming Cells of Birds.**—*Jl. Infect. Dis.* 1935. Nov.–Dec. Vol. 57. No. 3. pp. 315-336. With 2 coloured plates, 2 figs. & 3 charts. [34 refs.]

A study of the bird malarial parasite *Plasmodium elongatum* in experimentally infected canaries has shown that it has a 24-hour cycle, with a peak of segmentation between 8 and 10 o'clock in the morning. The most interesting feature of the parasite is that it is capable of living and developing in all blood and blood-forming cells of the canary, including the granular leucocytes. The vast majority of the parasites, however, occur in the cells of the erythrocyte series, while the gametocytes are found only in the normoblasts and erythrocytes. Those schizonts which occur in cells devoid of haemoglobin do not form pigment, which is present only in those growing in cells with obvious haemoglobin. Another peculiar feature is the shape of the merozoites, which are elongate and arranged like those of coccidia. The paper, which has two excellent coloured plates, describes the various types of cell in the bone marrow and spleen which are liable to contain parasites and their relationship to one another.

C. M. W.

Brumpt (Émile). Réceptivité de divers oiseaux domestiques et sauvages au parasite (*Plasmodium gallinaceum*) du paludisme de la poule domestique. Transmission de cet hématozoaire par le moustique *Stegomyia fasciata*. [**Susceptibility of Various Tame and Wild Birds to *Plasmodium gallinaceum*. Transmission by *Stegomyia fasciata*.**]—*C. R. Acad. Sci.* 1936. Oct. 19. Vol. 203. No. 16. pp. 750–752.

Working with a strain of *Plasmodium gallinaceum* imported from Ceylon the author has successfully maintained the strain by sub-

inoculation. He has shown that it is possible to infect the goose, pheasant, partridge and peacock but not the duck, guinea fowl, pigeon, quail, buzzard, canary, sparrow, calfat and chaffinch. In fowls a heavy infection, not infrequently fatal, follows inoculation. Development of the parasite does not take place in *Culex fatigans*, whereas in *Stegomyia fasciata* it occurs with the greatest ease, all mosquitoes exposed having become infected. In one on the eighth day 1,650 oöcysts were counted on the stomach. The author's opinion is that the fowl is not the natural host of the parasite, which in these birds is very limited in its distribution. *C. M. W.*

Taliaferro (William H.) & Cannon (Paul R.). **The Cellular Reactions during Primary Infections and Superinfections of *Plasmodium brasilianum* in Panamanian Monkeys.**—*Jl. Infect. Dis.* 1936. July–Aug. Vol. 59. No. 1. pp. 72–125. With 13 plates. [29 refs.]

This paper gives the results of an exhaustive investigation into monkey malaria from the point of view of the mechanism of natural and acquired immunity. The parasite, *Plasmodium brasilianum*, used in this study is of the quartan type in which the schizogony cycle is completed in 72 hours. The infections in various monkeys of Panama were produced as a rule by the intrave ous inoculation of several cc. of heavily infected blood. Parasites could be detected by the examination of thin blood films immediately after the inoculation, and the infection thus produced progressed steadily from this point till a crisis occurred. At the crisis the number of parasites in the blood decreased rapidly till a condition of low grade blood infection was reached. This passed into a latent phase during which parasites could be detected in the blood only during the spontaneous relapses of greater or less intensity. The blood and organs of some hundreds of monkeys thus infected were examined, parasite counts were made both in blood and agar smears, while frequently portions of spleen were removed during life with a view to observing in the individual animal the changes which were taking place during the course of an infection. The whole study has been most carefully carried out and confirms the conclusions reached from the previous studies on immunity in bird malaria. The paper, which is illustrated by a number of excellent plates depicting the cellular reactions and tissue changes, is one of the most important which have appeared on the subject of immunity in malaria. It contains so much detail that it will be possible to give here but a brief outline of its main contents.

It has been determined that throughout an infection in any individual monkey the rate of reproduction of the parasite is fairly constant, save for a slight retardation of the cycle at the time of the crisis from the normal three-day period to four days. This being the case, it follows that the variations in the number of parasites in the blood at different stages of the infection are due not to alterations in the rate of reproduction but to varying degrees of parasite destruction which involves both the free merozoites and the intracorpuscular stages of the parasite. It may be accepted that of the 8 to 12 merozoites produced at schizogony only 3 succeed in entering the blood corpuscles and of these 3 only about half on an average survive. This means that in the most acute infections the net increase of parasites at every sporulation before the crisis is only about 50 per

cent. During and after the crisis, except during the temporary relapses, the rate of destruction of parasites is much greater than this.

The most important organs showing definite cellular reactions are the spleen, liver and bone marrow, and these reactions are of two kinds : firstly the phagocytosis of parasites by differentiated macrophages and secondly lymphoid hyperplasia which appears to build a mesenchymal reserve from which further macrophages are evolved. During the acute rise of the infection, counts have shown that parasites were relatively more numerous in the peripheral blood than in the blood of the internal organs. The spleen has always shown the highest concentration, there being approximately 20 times as many parasites for any number of red blood corpuscles as in the peripheral blood. The liver and lungs gave a ratio of about one-third of this while the remaining organs, including the bone marrow, rarely showed a concentration greater than three times that of the peripheral blood. It is noteworthy that the spleen, which showed the highest concentration during the developing infection, was the organ in which the most intense phagocytosis occurred at the crisis. It has to be remembered that phagocytosis occurs to some extent during the development of the infection and involves infected as well as uninfected red blood corpuscles. This erythrophagocytosis, quite apart from the destruction of red blood corpuscles by the parasites, is probably an important factor in causing the anaemia of malaria. At the crisis the phagocytosis of infected cells is suddenly increased and is to be looked upon as an acquired immunity response in contrast to the phagocytosis which has gone on before the crisis and which is due to a natural immunity. In the spleen during the early developing infection, infected red blood corpuscles pass into the Billroth cords and thence into venous sinuses. As the infection proceeds the infected cells are held up to an increasing extent in the Billroth cords till when the crisis is approached the infected cells no longer pass on into the sinuses. They appear to be held in the cords by some affinity for the macrophages. There then follows, sometimes quite suddenly, an active phagocytosis on the part of the macrophages in the Billroth cords of the detained corpuscles. A similar phagocytosis occurs also in the liver and bone marrow, but it was not possible to determine in these organs whether or not there occurred at the crisis a regional distribution of parasites comparable with that seen in the spleen just prior to the initiation of active phagocytosis. The phagocytosis in the liver and bone marrow, when compared with that in the spleen, is of little importance from the point of view of immunity except after splenectomy, long continued infection or failure of the spleen to respond to an infection. The intense phagocytosis at the crisis reduces the infection to a low level, in spite of the fact that the parasites continue to reproduce at their original rate.

The pigment accumulating in the macrophages at the crisis is at first in the form of fine granules, but these soon show a tendency to coalesce into larger masses which appear to occur in a smaller number of macrophages. It seems that the pigment finally disappears a few months after a malarial attack. If a relapse occurs fresh granules appear in the macrophages and these pass through the same phases as those deposited at the first attack. The macrophages of organs other than the spleen, liver and bone marrow play hardly any part in the defence against malaria. With the development of macrophage activity lymphoid and myeloid hyperplasia occurs. Lymphoid

hyperplasia is first detected in the spleen and then, in the case of severe and prolonged infections, it extends to the liver, bone marrow and possibly the kidneys. Myeloid hyperplasia is represented by erythropoiesis. Lymphorrhexis also is always associated with severe malaria. When it is extensive the reticular cells of the spleen follicles are transformed into macrophages and become distended with lymphocytic fragments. This lymphorrhexis appears to stimulate lymphoid hyperplasia. Primarily there is an enlargement of the lymphoid follicles in the spleen due to increase in the medium lymphocytes and to a less extent of the reticular cells and large lymphocytes. The small lymphocytes progressively disappear from the follicles, one of the most striking results of the infection. With continued malarial stimulation the red pulp becomes infiltrated with basophilic cells (plasma cells or lymphocytic cells). In the follicles and in the red pulp there can be seen every gradation between lymphocyte and macrophage, an indication of the active production of phagocytes. The disappearance from the follicles of the small lymphocytes is due partly to their migration into the pulp of the spleen or their transformation into medium lymphocytes which increase by mitosis, migrate and hypertrophy into monocytoid cells and macrophages. Associated with the active development of the lymphoid follicles themselves there appear in the red pulp of the spleen basophilic cells collected into irregular islands and scattered evenly throughout the pulp. These cells are either all plasma cells, originating for the most part from small lymphocytes but also from medium and large lymphocytes, or all lymphocytes of the small, medium and large types, the medium being the most numerous. These two types of basophilia are designated the plasma cell type and the lymphocytic type. The significance of the first type is not understood, as the function of the plasma cell is not known. Apart from this the entire process in the spleen seems to be directed to the formation of lymphocytes and reticular cells which can be transformed into macrophages. These changes, as is to be expected, bring about varying degrees of splenomegaly.

In the bone marrow it is impossible to distinguish between the early stages of erythropoiesis, myelopoiesis and lymphopoiesis, but frequently a hyperplastic bone marrow will exhibit a great increase in one of these processes without any appreciable change in the other two. Owing to the difficulty of distinguishing lymphocytes from other stem cells of various blood elements a diffuse lymphopoiesis cannot be recognized. On the other hand there sometimes occurs a formation of large lymphatic follicles containing pronounced secondary nodules with many mitotic figures. This lymphoid hyperplasia occurred in only a few animals and was associated with similar accumulations in the cortex of the kidney and the lung. In the liver, when malarial stimulation has been marked, increase in the periportal tissue, or mantling, as it is termed, is found. This increase is due chiefly to medium lymphocytes. This mantling, however, is of rare occurrence, so that hepatomegaly must be attributed to cloudy swelling and increase in size of Kupffer cells resulting from phagocytic activity.

Certain experiments were carried out to test the behaviour of the tissues towards superinfections by injecting large quantities of washed infected red blood corpuscles during the latent phase. Generally the changes which occur are similar to those of the primary infection,

but they are instituted immediately so that the injected parasites are removed rapidly from the circulation by active phagocytosis.

The reason why the spleen, liver and bone marrow are the organs chiefly concerned with the protection against malaria is that in them there is direct contact between blood and macrophages and a slow circulation, but the reason for the increased phagocytosis associated with acquired immunity is not so easily explained. The most simple explanation would be the action of some opsonizing antibody, but there is little evidence that such an antibody exists. There is, however, an increase in the number of macrophages which from the evidence available have arisen, as noted above, by transformation of lymphocytes, which themselves increase greatly in number as a result of the lymphoid hyperplasia which occurs in the spleen and other organs under the influence of continued infection. As regards the replacement of erythrocytes this is limited to an increased erythropoiesis in the bone marrow.

It thus appears that immunity in monkey malaria depends on the rate at which the macrophages can phagocytize the infected red blood corpuscles. In natural immunity the rate of destruction of parasites is in most cases insufficient to prevent the development of the infection, but with the advent of the crisis and acquired immunity the capacity of the macrophages, now greatly increased in number as a result of lymphoid hyperplasia, to destroy parasites is increased to such an extent that the infection is checked and reduced to a low level. This property of rapidly destroying parasites, except during temporary relapses, is retained as an acquired immunity for some considerable time. *C. M. W.*

Jaswant Singh & Harbhagwan. **Failure to produce Infection in Two Species of the Lower Oriental Monkeys by the Injection of Malarial Sporozoites from Naturally Infected Anophelines.**—*Records of the Malaria Survey of India.* 1935. Dec. Vol. 5. No. 4. pp. 495–497.

Large numbers of actively motile sporozoites from the salivary glands of naturally infected Anopheles were inoculated in Ringer's solution into two monkeys (*Silenus irus* and *S. rhesus*) both by the intravenous and the subcutaneous routes. The animals were examined daily for two months without showing any evidence of infection. It is presumed with good reason that the sporozoites were those of human malaria. *C. M. W.*

Rodhain (J.). La réceptivité des singes africains au *Plasmodium knowlesi*. [**The Susceptibility of African Monkeys to** *Plasmodium knowlesi*.]—*C. R. Soc. Biol.* 1936. Vol. 123. No. 34. pp. 1003–1006.

The experiments described were designed to determine the pathogenicity of *Plasmodium knowlesi* for African monkeys. They were carried out on three *Cercopithecus cephus*, one *Cercopithecus griseo viridis*, two *Cercocebus fuliginosus lunulatus* and four *Papio jubilaeus*. An Indian strain of *Pl. knowlesi* was used. Before the experiment all the monkeys were submitted to a course of treatment with atebrin and plasmoquine to avoid the possibility of the results being complicated by the appearance of some latent natural Plasmodium

infection. The animals were infected by subcutaneous or intramuscular injections of blood rich in *Pl. knowlesi*.

All the four species of monkeys were found to be susceptible to infection. In *Cercopithecus griseo viridis* and in *Papio jubilaeus* the infection develops in an acute manner, with a massive invasion of red cells, ending in death with symptoms of haemoglobinuria. In *Cercopithecus cephus* infection is milder and develops in a chronic manner. By judicious drug treatment it is possible to change an acute infection of *Papio jubilaeus* into a chronic one. The author considers this species of monkey to be a better reservoir of virus than is *Macacus rhesus*. The appearance of sexual forms of *Plasmodium kochi* in one *Papio jubilaeus* infected with *Plasmodium knowlesi* shows that there is no cross immunity between these two parasites. *N. W.*

Mosna (Ezio). L'azione della chinina e dell'atebrin sul *Plasmodium knowlesi*. [**Action of Quinine and Atebrin on** *P. knowlesi*.]—*Riv. di Malariologia*. Sez. I. 1936. Vol. 15. No. 2. pp. 99–105. With 30 figs. on 1 plate. English summary (8 lines).

In comparing the action of quinine with that of atebrin on *Plasmodium knowlesi* in the monkey the author finds that a single dose of atebrin has a more decided action on the morphology of the parasite, its rate of growth and its disappearance from the blood than has a single dose of quinine, which, however, has similar but less marked effects. *C. M. W.*

Chopra (R. N.), Das Gupta (B. M.) & Roy (A. C.). **On the Mode of Action of Atebrin on** *Plasmodium knowlesi*—**a Preliminary Note.**—*Indian Med. Gaz.* 1936. Dec. Vol. 71. No. 12. pp. 710–712.

Half a cubic centimetre of defibrinated blood from a monkey heavily infected with *P. knowlesi* (680,000 parasites per cmm.) was mixed with 0·5 c.c. of atebrin solution, 1 in 25,000 of sterile physiological salt solution, and the mixture, after 24 hours' incubation, was inoculated subcutaneously into each of two *Silenus rhesus* monkeys. As a control, two monkeys of the same species were similarly inoculated with the same quantities of defibrinated blood mixed with normal salt solution. Both control monkeys showed very heavy infections which proved fatal. Both monkeys inoculated with blood that had been mixed with the atebrin solution remained well. No parasites were at any time found in their blood and cultural and inoculation experiments gave no evidence of infection. The action of atebrin on malaria parasites would thus appear to be a direct one. *N. W.*

Ruge (H.). Neuzeitliche Probleme der Malariaforschung. [**Recent Problems in Malaria Research.**]—*Deut. Med. Woch.* 1936. Nov. 13. Vol. 62. No. 46. pp. 1869–1872.

The author again deals with James's investigations on malaria which were discussed in a previous paper (this *Bulletin*, 1937, Vol. 34, p. 153).

In regard to malaria prophylaxis he considers that atebrin is a distinct advance on quinine. For successful prophylaxis the former need be given only twice weekly in doses of 0·01 gm., in badly infected areas it may be combined with 0·01 gm. plasmoquine twice weekly. It is not yet definitely determined that these two drugs are causal

prophylactics. The prophylactic treatment should be begun one week before entering the malarial area in order that the drug may reach a certain level in the blood, which prevents the sporozoites from entering the reticulo-endothelial system. *E. D. W. Greig.*

CHOPRA (R. N.) & ROY (A. C.). **On the Determination of Small Quantities of Atebrin in the Blood.**—*Indian Jl. Med. Res.* 1936. Oct. Vol. 24. No. 2. pp. 487–488.

"Accurately measured amounts of oxalated blood (about 2 c.c.) were allowed to soak into the strips of filter-paper contained in the inner tube of Vedder and Masen's (1931) apparatus as modified by Chopra, Roy and Das Gupta (1934). It was then put inside a desiccator containing sulphuric acid overnight. The next day the dry paper-strips were re-shuffled by means of a clean platinum loop and the tube was inserted into the outer jacket. Ether was poured through the top of the inner tube, so that after filling it up, it was allowed to overflow and fill nearly half the bulb portion of the outer tube. This was then connected to a reflux condenser through which cold water was allowed to circulate and it was immersed in a hot water-bath up to the level of the ether contained in the outer tube. After the extraction had been allowed to proceed for two hours, the inner tube was removed and the ether extract contained in the outer tube was heated to drive away the ether. The extracted atebrin was dissolved in 4 c.c. of N/10HCl by heating in a boiling water-bath. It was observed that though ether sometimes extracted a yellow pigment even from blood containing no atebrin, this yellow colouring matter was not dissolved in N/10HCl. The acid extract was then cooled in ice and filtered through a small Whatman filter-paper. Three c.c. of the filtrate were then accurately measured into one of a set of small test-tubes of uniform bore and all made of the same kind of colourless glass-tubing and to the others varying amounts of the standard atebrin hydrochloride solution in N/10HCl were added. The standard atebrin solution used contained 0·01 mg. of atebrin hydrochloride per 1 c.c. of the solution. The total volume in each tube was made up to 3 c.c. by the addition of varying amounts of M/10HCl. 0·1 c.c. of 20 per cent. caustic soda solution was next added to each tube followed by 0·5 c.c. of amyl alcohol and then thoroughly mixed. The test-tubes were left for some time on the table to allow the amyl alcohol layer to separate completely. The yellow colour of the solutions was completely taken up by the layer of amyl alcohol. The colour of the amyl alcohol layer in the unknown was compared with that in the standards against a white background, the tubes being looked through sidewise." *N. W.*

WHITE (R. Senior). **On Malaria Transmission in the Jeypore Hills. Part I. A Year's Dissection Results.**—*Records of the Malaria Survey of India.* 1937. Mar. Vol. 7. No. 1. pp. 47–75. With 1 fig. [18 refs.]

The Jeypore Hills, part of the Eastern Ghats, running parallel to the northern part of the Bay of Bengal, at a distance of from 30 to 100 miles from the coast, and inhabitated by aboriginal tribes, have always had an unenviable reputation for malaria. The Raipur-Vizianagram Railway was constructed through this country between 1925 and 1931 and the author of this paper was in charge of the anti-malaria measures involved. Protection work has continued uninterruptedly and a large mass of data regarding Anophelines has accumulated. At the 1,000 feet level, 6,944 dissections of twelve species of Anophelines have been made, *culicifacies*, *fluviatilis*, *varuna*,

minimus, *aconitus*, *jeyporiensis*, *splendidus*, *maculatus*, *theobaldi*, *jamesi*, *pallidus*, and *annularis*. The six first named species were alone found infected and of these only *fluviatilis*, *varuna* and *minimus* were infective, that is, showed gland infections. Only these three species appear to be concerned in the transmission of malaria in this region. There being no differences in their respective breeding places, and their infected and infective rates being almost identical, they can, for practical purposes, be treated as one, the *funestus* group. The most interesting and important fact that emerges from this interesting paper is that *culicifacies* plays no part in the local transmission of malaria, though it dominates the Anopheline fauna. Only three infected guts were found among 4,744 *culicifacies* dissected. The explanation of this local lack of pathogenic importance of *culicifacies* has not yet been elucidated. Cattle sheds have a special attraction as a resting place, and zoophilism may be the clue. As a second possible explanation the author suggests that *culicifacies*, like *maculipennis* in Europe, may be a mixture of sub-species. *N. W.*

Symes (C. B.). *Anopheles funestus* (**Giles**) **as a 'Domestic' Breeder.**—*Ann. Trop. Med. & Parasit.* 1936. Oct. 21. Vol. 30. No. 3. pp. 361–364.

In Malindi, a small town of 750 dwellings on the coast of Kenya, 80 miles north of Mombasa, *A. funestus* has been found breeding in wells. Most of the wells are from 15 to 30 feet deep and contain a foot or two of brackish water. Larvae have also been found repeatedly in domestic water containers of many kinds ; many of these larvae are brought in with the daily supply of water from the wells, but in houses with large tanks it is probable that continuous breeding goes on in the house. *N. W.*

Evans (A. M.) & Garnham (P. C. C.). **The** *Funestus* **Series of** *Anopheles* **at Kisumu and a Coastal Locality in Kenya.**—*Ann. Trop. Med. & Parasit.* 1936. Dec. 23. Vol. 30. No. 4. pp. 511–520. With 1 text fig. & 3 figs. on 1 plate.

Anopheles funestus, Giles, one of the widely distributed African malaria vectors, has long been regarded as a very variable species. In 1930, Leeson recorded from Southern Rhodesia ten distinct forms of wing pattern (*Bull. Entom. Res.*, Vol. 21, pp. 421–428). Since then, by examination of developmental stages and certain internal characters of females, it has been established that mosquitoes formerly included under this name are not one species, but several. The group has become known as the *funestus* series of *Anopheles*. One Anopheline, described and named by Leeson as *A. funestus* var. *rivulorum* (this *Bulletin*, 1935, Vol. 32, p. 804) has in this paper been raised to specific rank, and the authors describe all stages of two forms found in Kenya. The larvae of one form were taken among beds of water lettuce (*Pistia stratiotes*), the other from water free of this plant.

In places where *A. rivulorum* and *A. funestus* type form occurred together in Kenya, only adults of the latter were found in human dwellings ; the authors therefore believe that *rivulorum* does not play any important part in the transmission of malaria. In S. Africa de Meillon (this *Bulletin*, 1936, Vol. 33, p. 845) recorded similar

observations when comparing habits of *A. leesoni*, Evans (another member of this series) and *A. funestus* type form.

Evidence is gradually accumulating and may yet show that in this series of Anopheles the house-frequenting habit is entirely confined to the type form. More work is needed, particularly with regard to determinations of the kind of blood required by the various species and the natural infection rate among them. *H. S. Leeson.*

EVANS (A. M.) & SYMES (C. B.). *Anopheles funestus* **and its Allies in Kenya.**—*Ann. Trop. Med. & Parasit.* 1937. Apr. 8. Vol. 31. No. 1. pp. 105–112. With 3 figs. on 1 plate & 1 map.

"Three members of the *funestus* series, *A. funestus* type form, *A. rivulorum* and *A. leesoni*, can definitely be recorded from Kenya.

"In comparison with the common and widely distributed *A. funestus* type form, *A. rivulorum* and *A. leesoni* may be described as localized or rare.

"It is more than probable that in most parts of the Colony, at least, *A. funestus* type form is the only one of these three species which is found in appreciable numbers in huts or houses; thus there is little, if any, doubt that records of natural infectivity in '*funestus*' in the Colony do actually apply to the type form of this species.

"Many of the larvae raised from eggs at Kisumu were abnormal in having the paired platelets isolated from the main plate on some or all of segments IV–VI. This condition was extremely rare among caught larvae. Such specimens differ from larvae of *A. funestus* var. *confusus* in having the main tergal plates unusually narrow."

ECKSTEIN (Fritz). Experimentelle Beobachtungen an *Anopheles maculipennis*. [**Experimental Study of** *Anopheles maculipennis*.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Sept. Vol. 40. No. 9. pp. 381–395. [27 refs.]

The author presents an experimental study on two races of *Anopheles maculipennis*, hoping to lay bare the causes of their different geographical distributions.

It is known that speaking generally the race *atroparvus* has a coastal distribution, and that it sometimes breeds in brackish water: *messeae*, on the other hand, breeds in fresh water. Others have already shown, and it is here amply confirmed, that the larva of *atroparvus* is resistant to a higher concentration of salt than the other larva. This is true both of small and large larvae. [Some progress in understanding these observations might be made if the anal gills were studied as organs for the absorption of water, following the work of WIGGLESWORTH.]

The author then passes to a number of surface effects on water, which may clearly be of great importance to the Anopheles larva. He shows that if the surface is treated with some fine powder the larvae of *messeae* are more readily killed than those of *atroparvus* of the same age. This is shown with several different, apparently inert, powders, and with groups of larvae nourished in different ways. It appears that the death of the *messeae*, the cause of which remains obscure, is in some way related to the introduction of these powders into the tracheal system. The author is inclined to relate these observations to events which might be supposed to occur in nature, expressing the opinion that fine particles would float longer on brackish than on fresh

water, and suggesting that the larva of *atroparvus* resists powder because it is more habituated to a water surface which is dusty.

P. A. Buxton.

Missiroli (A.). Influenza di alcuni fattori climatici sull' *Anopheles maculipennis*. I. Nota. [**The Influence of Climate on** *A. maculipennis*.]—*Riv. di. Malariologia.* Sez. I. 1936. Vol. 15. No. 6. pp. 385–398. With 3 figs., 3 graphs & 1 chart. English summary.

The paper describes observations and experiments on adult *Anopheles maculipennis* in a tunnel which provided a natural gradient of climatic conditions.

The author constructed a tunnel about 7 feet high and nearly 20 yards long, with a rectangular bend at the end, so that the extremity was in complete darkness ; in this he set up a series of instruments which measured temperature and humidity at various points. The tunnel was partly divided into four sections, each of which had a characteristic range of humidity, temperature and light. In order to discover which of the sections was the one in which the adults would live longest the author reared specimens of *A. maculipennis* of two races, gave them a single meal of blood and put them in cages in different parts of the tunnel, and recorded the mortality daily. The number of specimens used was very small, and the experiment was not apparently repeated, but it appears that the insects lived longer in the deeper parts of the tunnel. In a second set of experiments specimens which had been reared and fed once, were kept in cages at different positions ; in this experiment it was observed again that the mortality was less in deeper parts of the tunnel than near the mouth, and regular observations on digestion and on the maturation of the ovaries were made. It was found that the ovaries matured most rapidly in the first section, and that they took progressively longer in the deeper parts of the tunnel. The result is rather unexpected because climatic conditions, as shown on the graphs which are reproduced in the paper, do not appear to differ greatly once one has passed beyond the first section of the tunnel. The author also liberated a number of mosquitoes in the tunnel, closing its door with a wire screen. They showed a definite preference for the second section and none of them rested in the fourth, completely dark, section. Later, as the eggs began to mature, the insects moved nearer and nearer to the entrance, so that apparently their behaviour is complex, depending to some extent upon their physiological state.

The author expresses the view that female *A. maculipennis* show a preference for the climatic conditions which are most favourable for the development of the ovaries rather than for the life of the individual. *P. A. B.*

Reuter (J.). Oriënteerend onderzoek naar de oorzaak van het gedrag van *Anopheles maculipennis* Meigen bij de voedselkeuze. [**A Preparatory Investigation on the Cause of the Behaviour of** *A. maculipennis* **in the Choice of Food.**] Proefschr. Rijksuniv. Leiden. 1936. 118 pp. With 6 figs. [5 pages of refs.] English summary. [Summarized in *Rev. Applied Entom.* Ser. B. 1936. Sept. Vol. 24. Pt. 9. pp. 223–225.]

" A given species or race of Anopheline can be of importance as a vector of malaria only if it maintains constant contact with man,

as otherwise it is likely to inoculate the sporozoites into animals. The reasons for a mosquito being zoophilous or anthropophilous have not been ascertained. The present thesis records work in Holland investigating whether food preferences exist and what stimuli induce feeding. The varieties of *Anopheles maculipennis*, Mg., used were *atroparvus*, van Thiel, and *labranchiae*, Flni., the first being known as zoophilous and the second as anthropophilous. The literature on food preferences of Anophelines is surveyed.

" The author's experiments were made under the direction of P.H. van Thiel and were exploratory in character, for a definite judgment would require many other tests and also comparisons with other species of mosquitos. The period of maximum activity (including feeding) of *atroparvus* was so short as to render it undesirable to devote any part of it to developing an appropriate technique, and for this reason preliminary tests during the semi-hibernation period of *atroparvus* were made with laboratory bred females of *Aëdes aegypti*, L., to find the stimuli causing them to seek blood. The technique thus worked out appeared suitable for *atroparvus* and was used during its active period.

" The females of *A. aegypti* were collected by introducing an arm into the breeding cage and were then immediately removed from the arm before they had sucked more than a negligible quantity of blood. The tests were made with an " imitation arm " fitted to one side of an iron gauze cage, so as to project horizontally into the interior. It consisted of a glass cylinder 18 inches long and 2 inches in diameter. Warm water, mixed to the desired temperature from cold and hot pipes, flowed into the cylinder at its outer end and was taken away at the inner end, the outflow pipe being bent downwards and back parallel to the cylinder until outside the cage beneath the inflow pipe. Two strips of filter paper about 2½ inches wide were hung on the arm so as to provide a rough surface. In tests on the effects of humidity and odours one strip was moistened with distilled water and the other with a solution of odoriferous substances. The outer surface of the paper was kept at 30–35°C. [86–95°F.], approximating to the temperature of the human arm.

" The various acids in human sweat did not attract *A. aegypti*. Moisture was distinctly attractive, and warmth was essential to induce feeding. When the water in the cylinder was at about 25°C. [77°F.] the mosquitos were quiet ; they became active when it was at about 28°C. [82·4°F.].

" For the experiments with *atroparvus*, the females were captured in pig-sties, and 50–75 were placed in the cage daily. Warmth was the foremost requirement, the mosquitos flying up and settling on the paper, which they tried to puncture, when water at 30–40°C. [86–104°F.] was passed through the cylinder. Moisture did not attract *atroparvus* so much as *A. aegypti*. No preference for any colour was observed with wet or dry white, grey or red papers. Tests were made with acids, human sweat, cotton wool rubbed on the skin of man and pig, pig faeces, skatol, indol, ammonia, human and pig blood, and with a human arm. The only distinct stimuli were produced by human and pig blood and pig faeces. It appeared very probable that temperature by itself was sufficient to cause feeding. In most tests *atroparvus* preferred the blood of pig to that of man, but sometimes the blood of a particular man was more attractive.

" Other experiments were made in which *atroparvus* was given the whole evening and night in which to make a food choice. The special cage used is described and the results are tabulated. There did not seem to be any definite food preference nor any attraction by sweat or the acids in sweat. In yet other experiments the females were placed in a cage midway between a wooden box containing a pig and one containing a man. The cage communicated with each box by means of a length of stove pipe, and the mosquitos were given the whole evening and night to make their choice. The results are recorded in detail. The pig was generally the more attractive, but individual attractiveness varied greatly. The choice appeared to depend primarily on temperature and to a less degree on air humidity. If the temperature stimulus was insufficient, an increase of humidity could reinforce it, but temperature was always required. In view of tests with an odourless attractant and of the fact that with an increase of humidity man could become as attractive as a pig, it appears that odour plays little if any part. It is suggested that the attractiveness of the pig is due to the enhanced warmth and humidity produced by it as compared with man, and that the character of a house or animal shed must be of importance.

" The same apparatus was used with var. *labranchiae* in experiments to test whether its reputed preference for feeding on man really existed. The mosquitos were bred from eggs received from Rome in July and August 1935. They did not appear to show a preference for man.

" In observations on *atroparvus* in the field, the mosquitos leaving and entering a pig-sty were counted, and the temperature and humidity were recorded. The mosquitos were most active between half-an-hour before and half-an-hour after sunset. At first they left the sty and later they sought to enter. They need stimuli in order to find food, and enter a pig-sty in the morning not primarily to find a host but for shelter. The temperature and humidity of the air streaming out of houses and sheds at the time of maximum activity are greater than that of the outer air, and these two factors probably suffice to attract *atroparvus* inside. The " malariousness " of small working class dwellings with many inmates is ascribed to the many mosquitos found there and to the ease with which a few mosquitos can infect several persons."

MER (G.). Variations saisonnières des caractères de *Anopheles elutus* en Palestine. II. [**Seasonal Differences in Morphological Characters of** *A. elutus* **in Palestine.**]—*Bull. Soc. Path. Exot.* 1937. Jan. 13. Vol. 30. No. 1. pp. 38–42. With 1 chart.

There is no doubt that many of the differences between races of *Anopheles maculipennis* are genetic, but it is also clear that within one race there is much variation, some of which is apparently due to seasonal changes in climate or water. The differences recorded in this paper should clearly be referred to the second category. The material which was studied consisted of specimens belonging to one race only (*elutus* or *sacharovi*) collected in a small area in Palestine.

The greater part of the present paper is a discussion of measurements of length of wing and of thorax of individuals collected in different months over more than one year. It is approximately true to say that in summer, when the water temperature is 25–26°C., the insects are

smaller than in winter (water temperature is 18–20°C), but the matter is complicated because in summer wings tend to be shorter relative to thorax. *P. A. B.*

Roubaud (E.) & Treillard (M.). Sur une variété portugaise de l'*Anopheles maculipennis* (groupe *atroparvus*). [**A Portuguese Variety of** *Anopheles maculipennis* (**Group** *atroparvus*).]—*Bull. Soc. Path. Exot.* 1936. July 8. Vol. 29. No. 7. pp. 726–730. With 2 figs.

At the end of this paper the designation *cambournaci* is proposed for what is the latest addition to the named races or varieties of *A. maculipennis*. The name chosen is in honour of Dr. F. Cambournac, who, from the region of Aguas de Moura, Portugal, forwarded by air to Paris, living adults which, 48 hours after their arrival at the beginning of March, obligingly produced batches of fertile eggs. The latter gave rise to a strain whereof successive generations have since been reared in the insectary. Though the eggs laid by the Portuguese females are, from their general appearance, clearly allied to those of *atroparvus*, with which they had previously been identified by local authors, they are at once distinguishable owing to the small size of the floats. This can be appreciated by comparing the float-indices (*i.e.*, mean ratios between length of float and total length of egg), which, according to country of origin, are as follows :—Portugal, 0·24–0·29 ; Vendée, 0·37 ; Holland, 0·40 ; Italy, 0·38. While the markings on the Portuguese eggs resemble those on the eggs of *atroparvus* fairly closely, and the intercostal membrane is smooth, the mean number of ribs in the floats is smaller—13 to 14, instead of 16 to 18. The float-characters in question have remained stable throughout many generations of the Portuguese strain, which were bred in Paris.

From the results of crossing experiments with French *atroparvus* it is likewise concluded that the smallness of the floats in the Portuguese type is a dominant genetic character, and that the Portuguese *maculipennis* represent a special variety or biotype, distinct from *atroparvus*, though closely resembling it in various morphological and biological details.

The Portuguese form is definitely zoophile ; its maxillary index is about 16, and, like *atroparvus*, it is stenogamous, *i.e.*, it breeds freely in confined spaces. Possibly differences from *atroparvus* will be found in its winter behaviour ; the fact that in the Paris laboratory, at the beginning of March and at normal indoor temperature, Portuguese females all oviposited after a single meal of blood seems to show that in them the winter diapause is subject only to temperature, and that homodynamy is the rule. Should this be the case, it would afford a further distinctive character between the two races. *E. E. Austen.*

Roubaud (E.) & Colas-Belcour (J.). Influence favorable d'une légumineuse fixatrice d'azote sur le développement d'un plankton nitrophile propice aux larves d'anophèles. [**Favourable Influence of a Leguminous Fixative of Nitrogen on the Development of a Nitrophilous Plankton propitious to Anopheline Larvae.**]—*Bull. Soc. Path. Exot.* 1936. July 8. Vol. 29. No. 7. pp. 798–805.

With the practical object of obtaining in suitable abundance batches of mosquitoes for use in transmission experiments, the authors,

working in the Entomological Laboratory of the Institut Pasteur, in Paris, tried various methods of rearing newly hatched larvae of *Anopheles maculipennis* var. *cambournaci* (*vide supra*). When the larvae were placed in solutions containing either nitrate of ammonium or acetate of soda, to the first of which a green Flagellate, *Euglena gracilis*, was added, while into the second the colourless Flagellate *Chilomonas paramecium* was similarly introduced, the Flagellates prospered, but results as regards survival and growth of the larvae were not satisfactory. The question arose whether, in natural breeding places, there are not definite associations between certain submerged plants and particular elements of the plankton, such as the Flagellates or certain types of algae, which result in conditions more especially favourable to easy, abundant and rapid development of the larvae. In this connection the authors' attention was directed to the part that may be played by leguminous meadow plants, which fix nitrogen, in supporting nitrophilous Protozoa, such as *Euglena*, which are among the regular constituents of the food of anopheline larvae. The attempt was then made to obtain a more suitable plankton by introducing clumps of white clover into jars containing tap water ; in the case of controls, sods of turf, sprouting lentils in pots of sand, or ordinary vegetable mould were employed in place of the clover. In each instance the tap water was charged with *E. gracilis*, *Ch. paramecium* or some other Flagellate, which, as in nature, assists in forming a superficial planktonic pellicle, whereon the larvae feed.

Details are given of three experiments, in each of which two or more jars were used. It was found that the media most favourable to the rearing of larvae of the strain of *A. maculipennis* employed were those in which the water had been charged with *Chilomonas* and *Euglena*, and provided with a clump of clover, either simply immersed in the liquid or placed in a pot. It is to be supposed that the clover, and indeed any leguminous fixative of nitrogen, diffuses round itself nitrates, which are utilized by the Euglenids and green algae, which serve to feed the larvae and supply the water with oxygen. White clover was employed because it was the only species available at the beginning of the experiments, and because it resisted partial submersion of its roots ; other leguminous plants, especially those which grow habitually in damp soils, would doubtless serve as well, if not better.

The authors add a footnote to the effect that, subsequent to the carrying out of the experiments described, they have applied the same technique to other races of *A. maculipennis*, with equal success.

E. E. A.

ROZEBOOM (L. E.). **The Life Cycle of Laboratory-bred *Anopheles albimanus* Wiedemann.**—Reprinted from *Ann. Entom. Soc. America*. 1936. Sept. Vol. 29. No. 3. pp. 480–489. With 1 chart.

Anopheles albimanus is a very important carrier of malaria in certain parts of tropical America. Its biology in nature is known in considerable detail. The present paper contributes detailed, quantitative studies made in the laboratory.

The paper contains a large body of numerical fact on the mortality and duration of life of different stages, the number of eggs that the female lays, the secondary sex ratio and similar matters. The work

was carried out at 80–86°F. (26·7–30°C.). The information is valuable, being based on very numerous experiments, but it can hardly be summarized. It is concluded that the female requires at least a week after emergence from the pupa and at least one blood feed before eggs are mature ; the egg stage occupies 40–48 hours, the larval stages generally 8–13 days, and the pupal 30–33 hours ; adults generally emerge in the afternoon or evening. As an approximate figure, one generation occupies 18–24 days. It has been observed that the female is particularly willing to take human blood after a batch of eggs has been laid, and it is suggested that this may bring her back to habitations after visiting the breeding place. *P. A. B.*

Baisas (F. E.) & Hu (Stephen M. K.). *Anopheles hyrcanus* **var.** *sinensis* **of the Philippines and Certain Parts of China, with Some Comments on** *Anopheles hyrcanus* **var.** *nigerrimus* **of the Philippines.**— *Monthly Bull. Bureau of Health.* Manila. 1936. June. Vol. 16. No. 6. pp. 205–242. With 6 plates & 2 figs. [52 refs.]

While the Oriental *A. hyrcanus* appears, like *A. maculipennis*, to include a number of varieties, the var. *sinensis* itself " exhibits the puzzling characteristic of being an efficient malaria carrier in some places and not in others." After studying batches of eggs from various localities, the authors write :—" Three distinct types of eggs can be recognized under the *sinensis*-group of China and the Philippines. First, the wide-decked variety which appears to be present in China, Indo-China, Japan, Hong Kong, Malaya, Borneo, and Sumatra, but not in the Philippines. We assume that this is the true *sinensis* of Wiedemann, and the one responsible for malaria transmission in nature. Second, the narrow-decked variety which is found in China and the Philippines. We believe this should be erected into varietal rank for which the name *lesteri* is proposed. And, third, the form having a deck intermediary in width between the two other varieties. This is so far reported only from the Philippines and corresponds to the one for which Baisas (1935) proposed the name *pseudosinensis*." There follow short, illustrated descriptions of these three types of eggs and of those of var. *nigerrimus*, which are indistinguishable from the eggs of *lesteri*, albeit in the other stages these two varieties are readily separable ; notes on collecting ; and details concerning the larvae, pupae and adults of the several varieties. The authors emphasize that " the best method in classification is to take into consideration all the characters found in the eggs, larvae, pupae and adults of a given species or variety." *E. E. A.*

Urbino (Cornelio M.). **The Eggs of Some Philippine Anopheles.**— *Monthly Bull. Bureau of Health.* Manila. 1936. July. Vol. 16. No. 7. pp. 261–275. With 1 fig. & 6 plates. [18 refs.]

From specimens deposited in captivity, illustrated descriptions are given of the eggs of the following :—*A. barbirostis* (types 1 and 2, and an unnamed variety) ; *A. hyrcanus* var. *sinensis* (with which var. *lesteri* of Baisas and Hu, *vide supra*, is treated as identical) ; *A. pseudobarbirostris* ; *A. minimus* var. *flavirostris* ; *A. filipinae* ; *A. mangyanus* ; *A. vagus* var. *limosus* ; *A. ludlowii* ; *A. litoralis* ; *A. subpictus* var. *indefinitus* (types 1, 2 and 3) ; *A. maculatus* ; *A. karwari* ; *A. annularis* ; *A. philippinensis* ; *A. kochi* ; and *A. tessellatus*. In addition, the eggs

of *A. hyrcanus* var. *nigerrimus* (which, in agreement with Baisas and Hu—again *vide supra*—it is stated cannot be differentiated from those of var. *sinensis—i.e.*, var. *lesteri* according to the authors in question) are figured but not described.

The above-mentioned descriptions are followed by a "Table for Separating the Eggs." *E. E. A.*

Kitchen (S. F.) & Bradley (G. H.). *Anopheles walkeri* **Theobald as a Vector of** *Plasmodium falciparum* **(Welch).**—*Amer. Jl. Trop. Med.* 1936. Sept. Vol. 16. No. 5. pp. 579–581.

It has been previously shown that *A. walkeri* is an efficient vector of *P. vivax*. This mosquito has recently been found in Central and Southern Florida. Nine of these Florida Anophelines were fed on a patient suffering from a *falciparum* infection whose blood contained very numerous gametocytes. As a control, twenty-six *A. quadrimaculatus* were fed on the same patient. Twenty *quadrimaculatus* became infected but only one *walkeri*. The infected *walkeri* developed only one cyst on the stomach. It is concluded that the southern form of *A. walkeri* is not an efficient vector of *P. falciparum*. *N. W.*

Earle (W. C.) & Howard (H. H.). **The Determination of Anopheles Mosquito Prevalence.**—*Bol. Asoc. Med. de Puerto Rico.* 1936. Oct. Vol. 28. No. 10. pp. 233–240. With 4 figs.

The determination of the density of Anophelines is of importance in most antimalaria campaigns. Regular catches of adult mosquitoes in certain fixed diurnal resting places is the method commonly adopted. The authors of this paper point out that the diurnal resting places of certain important malaria vectors in the tropics are not known. *A. albimanus* in Porto Rico is an example of such a vector; *A. grabhamii* is another. Most mosquitoes of this type are more or less zoophile. The method usually employed is only satisfactory for those mosquitoes that are definitely anthropophile.

The use of a trap with animal bait for studying the prevalence of *A. albimanus* in Porto Rico is described. Prolonged experience has demonstrated its value. *N. W.*

Earle (W. C.). *Anopheles grabhamii* **(Theobald), a Possible Vector of Malaria.**—*Bol. Asoc. Med. de Puerto Rico.* 1936. Oct. Vol. 28. No. 10. pp. 228–232.

A. grabhamii has been found only in the Greater Antilles and the Virgin Islands. Naturally infected specimens have been captured, but little is known of its importance as a malaria vector. The author has succeeded in infecting *A. grabhamii* with *Pl. falciparum* and the development of the parasite ran parallel with that in simultaneously infected *A. albimanus*, the most important local vector. He concludes that *A. grabhamii* may be a vector, but in Porto Rico, at any rate, it is not an important vector. It is not sufficiently prevalent and it is very markedly zoophile. It is capable of breeding in very densely shaded water. *N. W.*

Cauchi (J.), Sellers (W.) & Bunkall (J. D.). **A Method of testing Oils and Other Chemical Agents for killing Mosquito Larvae.**—*Bull. Entom. Res.* 1936. Dec. Vol. 27. Pt. 4. pp. 649-652.

Artificial mosquito-breeding pits two feet square are dug in low-lying ground where the water is very near the surface. They are dug of such a depth as to contain 8–12 inches of water. When breeding occurs its intensity is determined by taking four dips with a standard dipper, one along each side of the pit. The larvae are counted, roughly classified into culicines and anophelines, and returned to the pit from which they had come. It was found that 5 cc. of the larvicidal oil to be tested is a suitable amount for these areas of 4 square feet of water. After the larvicide has been applied the pit is covered with a specially made trap in which any adults that may emerge can be observed. No pit is used for more than one test.

The cover traps are constructed of ½ inch board and have the shape of a truncated pyramid. Each of its four sides measures 3 ft. at the base, 6 ins. at the top and 3 ft. 3 ins. along each side. On the top of the cover is a cylindrical wire-gauze trap with wooden ends. Two sloping glass strips are fixed over a circular hole 4 inches in diameter on the top of the pyramidal cover ; these glass slips are separated by an interval of ¼ in. along their upper edges. This slit is the only means whereby mosquitoes hatching in the pit can gain access to the trap. Each side of the pyramidal cover has a window 8 ins. by 7 ins. : two of these windows are of glass, two of perforated zinc sheeting. The cover is painted white inside and out.

The authors claim that these breeding pits enable the testing of larvicides to be carried out under more natural conditions than the laboratory affords. More reliable comparative results are obtained than by ordinary field tests : with these pits standard uniform conditions—area of water, quantity of larvicide, &c—are always secured.

N. W.

Ul'Yanishchev (V. I.) & Rifling (E. A.). **A New Preparation "Oleoarsenite" for Control of Mosquito Larvae.**—*Summary Sci. Res. Work Inst. Plant Prot. 1935.* Leningrad, Lenin Acad. Agric. Sci. pp. 473–475. [In Russian.] [Summarized in *Rev. Applied Entom.* Ser. B. 1937. Mar. Vol. 25. Pt. 3. p. 68.]

"Of various waste products of the oil-refining industry tested in the Azov-Black Sea Region as carriers for Paris green against Anopheline larvae, the best was oleogumbrin. This is a black powder, the particles of which average 15·85 microns ; it has a specific gravity of 0·7 and contains 10 per cent. of waste oil, which prevents it from being wetted and keeps it on the surface of the water as a thin film for a period of over 10 days. The addition of 4 parts oleogumbrin to 1 part Paris green decreased by from 20 to 50 per cent. the amount of Paris green required for a given area of water. In large scale trials, in which nearly 160 sq. miles of water surface were dusted, the mixture invariably gave 100 per cent. mortality of Anopheline larvae. To obtain a larvicide cheaper than Paris green, however, oleogumbrin was tested in combination with a calcium arsenite insoluble in water, but soluble in weak acids. A 1 : 4 mixture, which was named oleoarsenite, killed all Anopheline larvae in 5–10 hours when used in the laboratory, and was applied in the field with equally successful results, a water surface of about 60 sq. miles being dusted with it in the autumn of 1934. The preparation of the mixture is very simple, it floats well and costs much less than any larvicide containing Paris green."

COVELL (G.) & AFRIDI (M. K.). **Experimental Application of Paris Green from Aircraft.**—*Records of the Malaria Survey of India.* 1937. Mar. Vol. 7. No. 1. pp. 93–103. With 2 diagrams, 2 figs. & 1 plate.

These aeroplane Paris green dusting trials were carried out in the Bela, the Jumna river-bed, in close proximity to Delhi. A Fox Moth biplane was used for the experiments and a detailed description of the hopper attached to the machine is given. Soapstone powder which was used as a diluent for the Paris green was very satisfactory. Successful results were obtained but for many reasons, those of danger and relative cost being important, the authors do not consider the method to be one of practical value in India in present circumstances.

N. W.

MAIL (G. Allen). **Thiodiphenolamine—a New Ingredient of Mosquito Larvicides.**—*Jl. Econom. Entom.* 1936. Dec. Vol. 29. No. 6. pp. 1144–1146.

This is a contribution from Montana State College Agricultural Experiment Station. Thiodiphenolamine, $S(C_6H_4)_2NH$, is very soluble in benzene and acetone, soluble in ether, and slightly soluble in alcohol. The addition of a small quantity of this substance to an oil greatly increases its larvicidal potency. In one series of experiments a 5 per cent. solution of thiodiphenolamine in acetone was added to Diesel oil ; in another series a suspension of thiodiphenolamine in Diesel oil was used. In the latter experiment little difference was observed between the larvicidal action of a freshly mixed suspension and that of the supernatant liquid from such a mixture that had been allowed to stand for 24 hours. The protocol of this experiment is reproduced :—

Comparison of toxicities of freshly mixed thiodiphenolamine-Diesel oil, and mixture of same 24 hours old. Experiment started at 10.45 a.m. with 100 larvae to each dish.

Surface area of dish, sq. cm.	Material	cc. used	Per cent. dead at 11.45 a.m.	1.45 p.m.	2.45 p.m.	3.45 p.m.	4.45 p.m.
800	Diesel oil alone ...	0·3	6	10	22	40	55
800	Supernatant liquid from 100 cc. diesel oil + 0·5 gm. TDPA	0·3	47	89	98	99	100
721	Fresh suspension of 100 cc. diesel oil and 0·5 gm. TDPA	0·3	21	67	84	90	97

N. W.

SCOTT (David T.). **Malarial Control Measures by Vertical Drainage (Percolation Pits).**—*Proc. Ann. General Meeting Assam Branch Brit. Med. Assoc., Shillong, March 4, 5 & 6, 1936.* pp. 22–25. With 2 figs.

This paper describes the construction of percolation pits on a tea estate in the Bengal Dooars whereby breeding places of *A. minimus*

have been eliminated. Percolation pits must reach good stony pervious soil; in this case it was found at twelve feet. The water dealt with is the waste water from water tanks. The tank plinth leads into a concrete drain in the course of which there is a mud-trap which breaks the flow of water, thereby causing the deposition of silt. From the mud-trap the drain leads to a cattle-trough, the overflow from which goes to the percolation pit. The percolation pit is not filled with stones; stones were used at first but they quickly became covered with slime. The pits are covered and fitted with a well-fitting manhole and the lead-in drain is furnished with a self-acting flap. These latter precautions were found to be necessary to eliminate the breeding of culicines. *N. W.*

Ovtchinikov (K. M.), Tischenko (C. D.) & Morozova (L. I.). **Observations on the Effect of Different Rates of Flow in Canals and of Small Water-Falls on Larvae of** *Anopheles maculipennis.*—*Med. Parasit. & Parasitic Dis.* Moscow. 1937. Vol. 6. No. 1. [In Russian pp. 37–54. With 4 figs. English summary pp. 54–55.]

The minimum rate of flow usually recommended, 0·2 m. per second, will not prevent growth of vegetation and silting up of the canal bed; 0·25–0·4 m. is necessary, according to natural conditions. Flushing with a wave of speed 0·2–0·5 m. did not, in the authors' experiments, destroy larvae of *A. maculipennis*, except in the first stage; even repeated waves at definite intervals had little effect in shifting the larvae. Larvae passing through lock systems at flood gates and watersheds were destroyed by the fall up to 17–40 per cent., but the proportion destroyed varied greatly, 60 per cent. or so of those of the first instar, only 3·5 per cent of the second and third; it seems to depend on the fall, so that installation of a series of falls might be most beneficial in larval destruction. *H. H. S.*

Sotiriadès (D.). **Passive Immunity in Experimental and Natural Malaria.**—*Jl. Trop. Med. & Hyg.* 1936. Nov. 16. Vol. 39. No. 22. pp. 257–260. With 4 charts. [12 refs.]

The author states that during the past year he has studied the therapeutic action of the serum, or whole blood, of patients suffering from general paralysis, who had been treated some time previously with malaria-therapy (*P. vivax*), on other paralytics suffering from acute experimental malaria. It is difficult to draw conclusions from the details furnished of six such cases, each of whom received an injection of 20 cc. of blood. The author states that such an injection is followed by abatement of fever generally after the fourth or fifth bout. The work was done in Berlin in collaboration with P. Jossman. In three cases the blood was examined every three hours after the injection to determine the influence of such injection on the leucocytic formula; charts are given. In the cases observed the leucocytic formula remained within normal limits not showing the changes characteristic of tertian malaria. *N. W.*

Ashford (Mahlon). **The Nature of Immunity to Malaria in its Relationship to Anti-Malarial Therapy.**—*Amer. Jl. Trop. Med.* 1936. Nov. Vol. 16. No. 6. pp. 665–678. [13 refs.]

The author, justifiably confused by the puzzling contradictions contained in the reports of many competent observers regarding the

nature of immunity to malaria and the effect of drugs on such immunity, has confronted the opinions of some of the foremost authorities in this field. Summaries are given of the views of JAMES, CRAIG, RUSSELL (F. F.), CLARK, the League of Nations 1933 Report, GARNHAM, Gordon THOMSON, GILL and BOYD. As a result of this study the conclusion is reached that immunity to malaria has at least two elements, one plasmodicidal, the other antitoxic. The author thinks that conflict of opinion may be in part due to failure to recognize the dual nature of malaria immunity. *N. W.*

ESTER (Ferrando). Sul comportamento di alcune sieroreazioni della sifilide sul siero di sangue dei non luetici inoculati sperimentalmente con malaria terzana benigna. [**The Effects of Inoculated Malaria on the Serum Reactions in Non-Syphilitic Subjects.**]—*Giorn. di Batteriol. e Immunol.* 1936. Oct. Vol. 17. No. 4. pp. 502–517. English summary (9 lines).

The Wassermann, Müller and Sachs-Witebsky reactions were tried with the serum of ten non-syphilitics treated with therapeutic malaria with the following results. At the height of the febrile paroxysm the W.R. might prove positive (it did so in 8 of these) but administration of quinine brought it back to negative. [Positive reactions have been recorded in cases of malaria where there was no clinical indication or history of syphilitic infection.] Müller's reaction was positive in none of the cases, the Sachs-Witebsky was positive in four, and weak in a fifth. Hence in cases where a suspicious W.R. is obtained, confirmation or refutation should be sought by performing the other reactions and particularly the second. *H. H. S.*

VENOMS AND ANTIVENENES.

Césari (E.) & Boquet (Paul). Recherches sur les antigènes des venins et les anticorps des sérums antivenimeux (troisième mémoire). Venin de *Naja tripudians* et sérum anticobraique. [**On the Venom and Antivenene of** *Naja tripudians*.]—*Ann. Inst. Pasteur.* 1936. May. Vol. 56. No. 5. pp. 511-534.

This is a continuation of these authors' interesting series of researches on snake venoms. They have already considered those of *Vipera aspis* and *Cerastes cornutus* [see this *Bulletin*, 1936, Vol. 33, p. 384] and now report on similar investigations on the cobra di capello, *Naja tripudians*. They proceeded, as before, to determine the toxicity of the venom *in vivo* to rabbits, guineapigs and mice, when it is injected by the circulation or subcutaneously. They found that for the first two of these animals the toxicity is practically the same as those of *V. aspis* and *C. cornutus*, but is less for mice. Next the anticoagulant action *in vitro* was studied and the haemolytic properties estimated. The cobra venom has a high potency in this respect, so minute a quantity as 0·000005 mgm. sufficing ; this haemolytic action is destroyed by being heated to 100°C., much reduced by 90°C. ; hardly at all affected at 80°C. The authors next determined the antitoxic titre on its own venom, using the same three animals, rabbits, guineapigs and mice, and then the antitoxic properties, if any, of the cobra antivenene to the venom of *V. aspis* and of *C. cornutus* and, *vice versa*, of each of the two last antivenenes to the *Naja tripudians* venom. For details, the original article must be consulted ; the results are given in protocols. The results may be briefly summarized :—

Neither the anticoagulant nor the antihaemolytic potency corresponds with the antitoxic titre of the antivenene, nor does the precipitation or flocculation reaction give any criterion of the antitoxic properties. In fact, there is at present no means of estimating the therapeutic value of an antivenene except the crucial animal test of determining the dose which will bring about recovery from an otherwise fatal dose of the venom. The cobra antivenene has an action on *V. aspis* and *C. cornutus* venoms, though to a smaller degree than on the homologous venom. Though the coagulant diastatic principle is common to all, nevertheless, as in the case of the Viper and Cerastes, the coagulation of the blood plays no part in the toxic effects. The investigation points to the fact that there is a certain conformity in the antigenic constitution of the three venoms, that snake venoms contain an "antigen mosaic" whose constituents differ in their nature and action and thus, according to the predominance of one or other, give rise to the typical characters of certain venoms. This leads to a conclusion at variance with that of Calmette and Arthus that the antivenenes are strictly specific. They end the article with these words : Research, now in progress, on the properties of mixed antivenes obtained by the combined venoms of *Bitis arietans* and *Sepedon haemachates* [*i.e.* a Viperid and a Colubrid] will show better still the correlations in antigenic constitution of the venoms of different species of snakes. This will be the subject of a future report.

H. H. S.

GANGULY (S. N.) & MALKANA (M. T.). **Studies on Indian Snake Venoms. Part I. Daboia Venom : its Chemical Composition, Protein Fractions and their Physiological Action.**—*Indian Jl. Med. Res.* 1936. Apr. Vol. 23. No. 4. pp. 997–1006.

This is the first of a series of studies being carried out at the Central Institute, Kasauli. The authors show that in addition to colouring matters, daboia venom has as constituent elements, C,H,N,S and O, no phosphorus. They made determinations of the protein fractions, estimating the globulin, albumen and proteoses. The dried venom was found to contain 96·8 per cent. protein (15·5 per cent. protein nitrogen) and lipoids soluble in ether 2·8 per cent. ; globulin 23·3, albumen 22·1 and proteoses 50·5 per cent. The neurotoxic action was tested on pigeons, the haemorrhagin on white rabbits, the coagulant action on sheep's blood, for locating the active principles in the venom fractions. These three actions are attributed to secondary proteoses. Attempts were made to separate the active principles of the venom by various absorption methods and by fractional precipitation with Am_2SO_4 and precipitation with acetone. These have not yet been successful. *H. H. S.*

GANGULY (S. N.) & MALKANA (M. T.). **Studies on Indian Snake Venoms. Part II. Cobra Venom : its Chemical Composition, Protein Fractions and their Physiological Actions.**—*Indian Jl. Med. Res.* 1936. July. Vol. 24. No. 1. pp. 281–286.

Having studied the chemical composition of Daboia venom, the authors have turned their attention to the venom of the Indian cobra. The elements present were the same—C,H,N,S and O—and, in addition, phosphorus. Identification of the proteins was undertaken and these were found to be albumen and globulin as coagulable proteins, and primary and secondary proteoses as incoagulable. Though phosphorus was present in the venom, no phosphoproteins were discoverable. Extraction with ether removed a dark brown viscid substance—a mixture of lecithin and cholesterol. Analysis of the protein proved the composition to be : Albumen 39·69, globulin 20·31, primary proteose 11·31, secondary proteose 16·81, together with lecithin, cholesterol, inorganic substances and colouring matter.

As a result of testing the physiological action of the various fractions, the authors found that the fraction obtained by saturation with Am_2SO_4, representing the total proteins, contained the full toxicity, gauged by the effect in pigeons (the usual method at the Kasauli Institute for testing the neurotoxic action), while that separated by half saturation with Am_2SO_4 or full saturation with NaCl had no effect ; the pigeons survived intramuscular injection of ten times the m.l.d. Further tests demonstrated that the toxicity of the venom was associated with the secondary proteose, but, in contrast with that of *Daboia*, is thermostable to a great extent. Hydrolysis of the proteose deprives it of all toxicity. *H. H. S.*

GANGULY (S. N.). **Studies on Indian Snake Venoms. Part III. Enzymes in Daboia and Cobra Venoms.**—*Indian Jl. Med. Res.* 1936. July. Vol. 24. No. 1. pp. 287–294.

An interesting sequel to the foregoing studies. The proteolytic enzymes were tested upon gelatin, crystallized egg-albumen, casein

and fibrin; its powers of hydrolysing lecithin and of curdling milk were also investigated.

The author found that both venoms—cobra and daboia—would digest gelatin and egg-albumen to a degree comparable with the action of pepsin or papain, but less than that of trypsin, the cobra venom being more powerful than the daboia. The same held good as regards the action on casein in an alkaline medium. Both will digest fibrin. As regards lecithin, a lecithin-splitting enzyme was found in both venoms, more in that of the cobra. The cobra venom also has a powerful rennetic activity, that of daboia none.

Finally, the action of the homologous antivenenes on the enzymes was tested *in vitro*. It was found that the proteolytic action is not neutralized, but the rennetic action of the cobra venom is neutralized. One cc. of Kasauli bivalent antivenene neutralized the milk clotting enzyme of 20 mgm. of the venom. *H. H. S.*

GANGULY (S. N.). **Studies on Indian Snake Venoms. Part IV. Mechanism of the Coagulant Action of Daboia Venom on Blood.**—*Indian Jl. Med. Res.* 1936. Oct. Vol. 24. No. 2. pp. 525–529.

The theory in general acceptation at the present day regarding coagulation of normal blood is representable by the following scheme :—

$$\text{Prothrombin} \xrightarrow[\text{Thrombokinase}]{\text{Ca}} \text{Thrombin (A)}$$

$$\text{Thrombin} + \text{Fibrinogen} \longrightarrow \text{Fibrin (B)}$$

The author prepared the prothrombin, thrombin, thrombokinase (platelets) and fibrinogen in a pure state with a view to finding out whether Daboia venom in bringing about coagulation plays a part in stage A or B. The experiments are detailed and the author concluded that the venom of *V. russelli* does not convert prothrombin to thrombin nor fibrinogin to fibrin; it acts as a lytic on the platelets, thereby liberating thrombokinase, as represented thus :—

$$\text{Prothrombin} \xrightarrow[\text{Thrombokinase}]{\text{Ca}} \text{Thrombin (A)}$$

$$\text{Daboia venom} + \text{platelets}$$

Next, since moccasin venom possesses an antithrombin action, test was made to see whether this action could be neutralized by the venom of Russell's viper. The results, as shown in a protocol, suggest that either the Daboia venom can neutralize the antithrombic action of about twice the quantity of moccasin venom, or, if sufficient of the former is used, rapid conversion of prothrombin into thrombin occurs in such a quantity that the antithrombic action of the latter (moccasin venom) is counteracted. Further experiment showed that Daboia venom had no neutralizing action on the antithrombic property of moccasin venom, and the action of the former on blood was not that of neutralizing antithrombin. *H. H. S.*

GANGULY (S. N.). **Haemolysis by the Venom of the Indian Cobra** (*Naja tripudians*).—*Indian Jl. Med. Res.* 1937. Apr. Vol. 24. No. 4. pp. 1165–1174. With 3 graphs.

The author has investigated the haemolytic action of *Naia tripudians* venom fractions on the erythrocytes of guineapig, monkey, horse, and man, using globulin, albumen, and primary and secondary proteose fractions and also the venom after extraction of phospho-lipoids. He then estimated the effects on the haemolysis of varying the lecithin and cholesterol content of the haemolytic system, with whole blood and with the red corpuscles of the same animals and of rabbit and sheep. The results are presented in graphs and protocols and summarized by the author as follows :—

" The haemolytic action of cobra venom is associated with a fraction composed of globulin and primary proteose. It has been demonstrated that lecithinase accompanies this fraction,

" Quantitative studies on cobra venom haemolysis with this fraction on the blood of different animals have shown that the percentage haemolysis of whole blood is roughly in inverse proportion to cholesterol content. No exact relationship has been shown between haemolysis and relative content of cholesterol and lecithin within certain natural ranges, but where cholesterol is in large excess of lecithin, venom haemolysis as a rule is slight in case of whole blood. This relationship is not shown in the case of washed cells where other factors may be concerned in the haemolysis."

H. H. S.

BINET (Léon), WELLER (Georges) & JAULMES (Charles). Le pouvoir antitoxique du glutathion. Recherches sur le venin de cobra. [**The Antitoxic Action of Glutathion on Cobra Venom.**]—*C. R. Acad. Sci.* 1937. May 19. Vol. 204. No. 20. pp. 1513–1514.

The antitoxic action of glutathion in mineral poisoning has been noted by several writers ; the present paper deals with its effects relative to cobra venom. The test animal was the adult guineapig of 300-400 gm. weight. The venom was administered subcutaneously after solution in distilled water [the species of venom is not mentioned] ; the venom in doses of 0·25 mgm. per kilo proved fatal to controls in 4–6 hours, and this was taken as the m.l.d. For the experiments aqueous solutions of reduced glutathion were used, 40 mgm. added to an amount of dried venom corresponding to 0·33 mgm. per kilo, the mixture made up to 1 cc., neutralized and left for an hour at laboratory temperature before being injected. The onset of symptoms was retarded and some animals survived. At first the neutralization was effected with bicarbonate of sodium, but as this was slow to stabilize, trisodium phosphate was used for later tests.

In a second series of experiments the mixtures of reduced glutathion and venom were adjusted colorimetrically to a definite pH, ranging between 6·6 and 8·4, by 10 per cent. trisodium phosphate. The results were survival of animals injected with mixtures of pH between 7·4 and 8·4, death of those receiving mixtures below 7·4 but with some delay in onset of symptoms. There is manifested, therefore, *in vitro* at least some antitoxic action. *H. H. S.*

Taylor (J.), Mallick (S. M. K.) & Ganguly (S. N.). **Preservation of Coagulant Solutions of Daboia Venom.**—*Indian Jl. Med. Res.* 1936. Oct. Vol. 24. No. 2. pp. 521–524.

Daboia venom has proved its value as a haemostatic in haemophilia and other causes of bleeding. The dried venom is not always at hand or readily procurable and even if this difficulty is surmounted it is not always practicable to make up on the spot the high dilution necessary for therapeutic use. Hence the value of a stable solution of reliable coagulant potency. The authors have experimented with the following solutions :—

1. 1 in 500 aqueous solution of the venom with an equal quantity of glycerine, *i.e.*, a final strength of 1 in 1,000.
2. 1 in 1,000 aqueous solution in an atmosphere of CO_2.
3. The same concentration with addition of 0·4 per cent. tricresol.
4. The same aqueous solution plus 1 in 10,000 mercurial preservative (as used for sera and other biological products).

It was found generally that deterioration of coagulant activity corresponded closely with loss in toxicity. The authors concluded that the first of the above retains the coagulative power and is highly active in a dilution of 1 in 10 (*i.e.*, 1 in 10,000 of the venom). *H. H. S.*

Taylor (J.) & Mallick (S. M. K.) **The Action of Rattlesnake and Mocassin Venoms as compared with Indian Viper Venoms.**—*Indian Jl. Med. Res.* 1936. July. Vol. 24. No. 1. pp. 273-279.

Following up previous work [see this *Bulletin*, 1936, Vol. 33, p. 387] the authors have made a study of the venoms of *Crotalus adamanteus* and *Ancistrodon piscivorus* from America, in respect of their neurotoxic, haemorrhagic and blood-coagulant actions, as compared with those of the *daboia* (*V. russelli*) and *E. carinata*. They find that the haemorrhagin content of the American snakes is similar to that of the Indian phoorsa (*Echis*) but ten times that of *daboia* ; the haemorrhagin of all four is, however, of the same nature and is therefore neutralized by the *daboia* antivenene. The *daboia* has twenty times and the *echis* four times the neurotoxin content of the Crotalus venom ; that of the moccasin (Ancistrodon) is, in this regard, half that of Crotalus ; moreover the neurotoxins of the American species examined differ specifically from those of the two Indian species and are consequently not neutralized by the antivenenes of the latter. *Crotalus adamanteus* venom has a coagulant action but is much below that of *V. russelli* or *E. carinata* in high dilutions and this action is not neutralized by *daboia* antivenene. *H. H. S.*

Peck (Samuel M.), Rosenthal (Nathan) & Erf (Lowell). **Purpura. Classification and Treatment, with Special Reference to Treatment with Snake Venom.**—*Arch. Dermat. & Syph.* 1937. May. Vol. 35. No. 5. pp. 831–864. With 14 figs. [26 refs.]

This article is replete with information and more than one reading is needed if its full value and significance are to be grasped. The varied nature of purpuric manifestations is dealt with, the procedures for studying the blood and the capillaries and a detailed description of the intradermal venom test with moccasin venom—injection of 1 or 2 units of haemoglobin, the result being noted in an hour or a little under. In a table is set out the relationship of haematologic and

dermatologic purpura to moccasin venom intradermally administered. The histology of the various purpuric conditions is somewhat condensed and would be worth amplifying in a separate paper, but is included in order that the action of the venom can be demonstrated in treatment.

For therapeutic purposes, the initial dose for those under ten years of age was 0·2 cc. of a 1 in 3,000 dilution, and increased to a maximum of 1·0 cc. For adults these doses were doubled. Treatment was usually given twice weekly in arm or thigh. An ecchymosis might develop in the first 24 hours, and some patients showed hypersensitivity after 10–14 days' treatment, when desensitization might be called for. Some typical clinical records follow, with a discussion on the use of the moccasin venom for diagnosis, prognosis and treatment. The paper was followed by an interesting discussion, and in his reply Dr. Peck explained that his procedure was basically a titration of the haemorrhagins in the venom and that cobra venom did not give a positive reaction because it was deficient in the haemorrhagins though rich in haemolysins. Later, he proposes to undertake a chemical fractionation. *H. H. S.*

GRASSET (E.). **On the Interrelation of the Antigenic Properties of Snake Venoms and its Bearing upon the Polyvalence and the Assay of Sera.**—*Quarterly Bull. Health Organisation. League of Nations.* Geneva. 1936. June. Vol. 5. No. 2. pp. 367–390. [55 refs.]

Tests carried out in cross-neutralization of venoms have shown the necessity of preparing specific antibodies not only of the two groups Viperidae and Colubridae, but of their chief subfamilies and genera, *e.g.*, against the venoms of European vipers, North African Cerastes, South African Bitis, Indian *V. russelli* and Lachesis and Crotalines of South America. Though some of these have a common antigenic nucleus, they differ in secondary antigenic fractions. Studies of the effects of antivenenes of one species against the venom of another have been made and recorded [see this *Bulletin*, 1936, Vol. 33, pp. 382, 398]. If one of the antigens used comprises the fractions contained in the other venoms, group and generic neutralization will be greater and more easily obtained. Further " the relation in which group antigenic properties stand to special individual antigenic properties can be shown by testing sera prepared with single venoms for their specific neutralizing power against that particular antigen and also for their comparative group neutralization power against the other venoms of the group or species concerned."

CALMETTE concludes from his investigations that the neurotoxic function of all the reptilian poisons is identical. The South African antivenene has a higher neutralizing effect on the Indian cobra venom, *N. tripudians*, than upon the Cape cobra venom, *N. flava*, used in its preparation, but the reverse of this holds good as regards the Indian serum. Therefore, the African *N. flava* venom has a higher specific and group antigenic potency than that of *N. tripudians* [see GRASSET and ZOUTENDYK, this *Bulletin*, 1936, Vol. 33, p. 382]. By determining test doses of the different venoms relative to the antivenene unit adopted for these specific sera, and carrying out assays of the polyvalent serum in relation to these test doses, it will be possible, says the author, to estimate the antibody content of this serum in terms of

anti-Cobra and anti-Bitis units, and the assay of antivenenes in relation to standard sera has many advantages, theoretical and practical, over direct neutralization tests and an international standardization of antivenenes analogous to that of bacterial antitoxins would provide a satisfactory reference standard; the choice of animal (rabbit, pigeon, mouse), the temperature at which and the length of time during which the mixtures are allowed to stand, in fact, the technique generally and in detail, must be decided upon as necessary preliminaries. *H. H. S.*

CÉSARI (E.) & BOUQUET (Paul). Recherches sur le venin de la vipère lébétine (*Vipera lebetina*). [**On the Venom of *Vipera lebetina*.**]—*C. R. Soc. Biol.* 1937. Vol. 124. No. 4. pp. 335–337.

The venom with which the authors worked was a mixture from about a hundred of these snakes captured in Algeria. Four mgm. injected into the vein of a 2 kgm. rabbit proved fatal in 10 hours, 8–10 mgm. in less than an hour. Post-mortem, small haemorrhages were found in the subcutaneous tissue, intestine, diaphragm and pericardium; the peritoneum contained several cc. of blood, the ureters also were full, the lungs and kidneys pale.

Of other venoms, the fatal doses for rabbits weighing 2 kgm. were *V. aspis* 0·7 mgm., *Cerastes cornutus* 1 mgm., *Bitis arietans* 2 mgm. Clinically, the symptoms of poisoning by *V. lebetina* resemble those of *B. arietans* rather than those of the other two, which produce death in 5 minutes with massive coagulation of the blood.

The guineapig is more susceptible to *V. lebetina* venom than is the rabbit; 0·4 mgm. kills a 400 gm. guineapig in about 30 minutes; for a mouse of 20 gm. the fatal dose is 0·05 mgm. into the caudal vein, 0·1 mgm. subcutaneously.

The authors, having no specific antivenene at hand, tested the action of others, using two fatal doses, 4 mgm. per kilogram body weight, and varying amounts of antiserum obtained from horses, injecting after leaving them in contact at 37°C. for half an hour. They found that *V. aspis* antivenene, of which 0·3 cc. neutralizes 1 mgm., had to be given in doses of 3 cc. to neutralize 1 mgm. *V. lebetina* venom; a mixture of *B. arietans* antivenene, of which 0·4 cc. neutralizes 1 mgm., and *Sepedon haemachates*, of which 2·8 cc. neutralizes 1 mgm., had to be given in a dose of 4 cc. to neutralize 1 mgm. of *V. lebetina* venom; *Naja tripudians* antivenene, of which 1 cc. neutralized 1 mgm., had to be given in a dose of 1·5 cc. against 1 gm. of *V. lebetina* venom. Of the three antisera tried, therefore, the last proved the most potent. *H. H. S.*

MERCHANTE (F. R.). Composition des venins de serpents et action comparative des globulines et albumines. [**Composition of Snake Venoms and the Actions of the Globulins and Albumens compared.**]—*C. R. Soc. Biol.* 1936. Vol. 122. No. 19. pp. 487–489.

Briefly stated, the author's methods were as follows: The nitrogen was estimated by the Kjeldahl process, the non-protein nitrogen after removal of albumen by sulphosalicyclic acid, the water by drying for 3 hours at 110°C., ash by weighing after calcining, the sulphur by Benedict's method, tyrosine and tryptophane by that of

Folin and Marenzi, cystine by a modified process of the same workers. The albumens and globulins were separated by Howe's method: 25 mgm. of the venom were dissolved in 1 cc. of salt, 0·9 per cent., and to this was added anhydrous sodium sulphate 24 cc. of a 22·2 per cent. solution. In a table are given the results in grams per cent. of the venom, for six species of Bothrops, *Crotalus horridus*, *Trimeresurus flavoviridis*, *Daboia russelli*, and *Naja naja*. The albumens were found to be more abundant than the globulins, the percentage of tyrosine was about that of other proteins, tryptophane and cystine in larger proportion. The proteolytic and local actions are chiefly due to the albumen fraction and the clotting of milk, which was tested, due to the globulin fraction. The haemolytic action, the toxic (tested on the pigeon) and the reduction of blood tension (tested on the dog), was shared by both fractions, the albumen being a little more powerful. The coagulant action was due rather to the albumen fraction, but weight for weight the globulin fraction was more potent in this respect. *H. H. S.*

Ghosh (B. N.) & De (S.S.). The Migration of the Toxic Constituents of Cobra (*Naja naja*) Venom at Various pH in an Electric Field.—*Indian Jl. Med. Res.* 1937. Apr. Vol. 24. No. 4. pp. 1175–1182. With 1 diagram.

Suzuki (Chikashi) & Sugio (Kazuo). On the Relationship between Snake Venom and Bactericidal Complement. Observations into the Structure of the Bactericidal Portion of Complement as well as Notes upon the Theory of the Multiplicity of Complement.—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1936. Sept. Vol. 35. No. 9 (378). [In Japanese pp. 1965–1989. [28 refs.] English summary pp. 1989–1991.]

Holden (H. F.) & Setter (C. G.). The Ultra-Violet Absorption Spectra of Snake Venoms.—*Australian Jl. Experim. Biol. & Med. Sci.* 1935. Dec. 16. Vol. 13. Pt. 4. pp. 223–228. With 5 graphs.

Holden (Henry Francis). The Absorption Spectra of Some Modified Snake Venoms.—*Australian Jl. Experim. Biol. & Med. Sci.* 1936. June. Vol. 14. Pt. 2. pp. 121–130. With 7 graphs.

Tetsch (Chr.) & Wolff (K.). Untersuchungen ueber Analogien zwischen Bienen- und Schlangen(Crotalus)-Gift. [**On the Analogies between the Venoms of the Rattlesnake and the Bee.**]—*Biochem. Ztschr.* 1936. Nov. 10. Vol. 288. No. 1–2. pp. 126–136. With 7 figs. [Refs. in footnotes.]

It has been noted by several authors (Essex, Markowitz and Mann) that the action of bee-venom injected intradermally was almost identical with that of Crotalus venom and histamin. The authors have therefore undertaken a chemical analysis of these poisons in order to compare them and also made certain biological tests. Bee-venom was found to contain, in percentages, 43·6 carbon, 13·6 nitrogen, 7·1 hydrogen and 2·6 sulphur. That of *Crotalus terrificus* 44·9 C., 14·7 N., 6·6 H., and 3·6 S., while that of Cobra [species not mentioned] gave 45·2 C., 14·7 N., 7·0 H., and 5·5 S. The lethal doses for mice were respectively 6–10, 0·7 and 0·12 mgm. per gm. It will be noticed that the chief differences were in the

amounts of sulphur, and that the toxicity increased directly with that content.

Experiments carried out on the intestine of guineapigs with the whole venom and with fractions from the picrates showed that the bee-venom differed from that of Crotalus in containing a substance having a histamin-like action. *H. H. S.*

Havemann (R.) & Wolff (K.). Zur Frage der Eiweissnatur des Bienen- und Crotalusgiftes. I. [**On the Albuminous Nature of Bee- and Rattlesnake Toxins.**]—*Biochem. Ztschr.* 1937. May 19. Vol. 290. No. 5–6. pp. 354–359. With 4 figs. [19 refs.]

By means of cataphoresis the authors demonstrated the amphoteric nature of a fraction of bee venom and of Crotalus venom [in neither is the species tested mentioned]. They regard this reaction as strongly indicative of their albuminous nature. The isoelectric point of the bee venom is at pH 8·7, that of Crotalus 7·8. The cataphoresis results were confirmed by titration. Bee venom is soluble with difficulty in alkaline fluids at pH 8·3; that of Crotalus only slightly at about its isoelectric point. Both dialyse readily through collodion and parchment. *H. H. S.*

Kellaway (Charles H.) & LeMessurier (D. H.). **The Vaso-Depressant Action of the Venom of the Australian Copperhead** (*Denisonia superba*).—*Australian Jl. Experim. Biol. & Med. Sci.* 1936. Mar. Vol. 14. Pt. 1. pp. 57–76. With 13 figs. [12 refs.]

Intravenous injection of moderate doses of venom of *Denisonia superba* (Australian copperhead), or *Acanthopis antarcticus* (death adder), which have no coagulant principle, causes a temporary fall of blood pressure, but a second dose has no effect. Desensitization can be produced by repeated injection of minute doses. The authors in the present article analyse this vaso-depressant action of the venom, employing chiefly cats for their experiments, but also monkey, dog, rabbit and guineapig. The effects were tested on anaesthetized cats, on decerebrate or decapitated preparations and on animals with vagi divided and carotid sinuses put out of action; also on curarized and atropinized animals and on isolated heart-lung cat preparations and others.

The authors found that desensitization with venom does not alter the animal's response to other pressor or depressor substances. The initial fall of blood pressure is not related to the curari-like action of the venom, nor to by-products of coagulative changes due to traces of thrombin in the venom. A possible hypothesis of the vaso-depressant action and stimulant action on plain muscle was that they might arise from liberation of histamine by the lytic action of the venom on the cells, but no histamine could be detected in the perfusate from a cat's lung following administration of venom; the effects are more probably the result of direct action of the venom on plain muscle. The article is illustrated by good blood pressure tracings. *H. H. S.*

Akatsuka (Keiji). **Immunological Studies of Snake Venoms.**—*Japanese Jl. Experim. Med.* 1936. Apr. 20. Vol. 14. No. 2. pp. 147–183. [27 refs.]

The author has carried through an intricate piece of work in attempting to immunize certain animals—mice, guineapigs, rabbits

and horses—against the venoms of *Lachesis flavoviridis*, *Naja tripudians*, and precipitin experiments were also performed with the venoms of *Bothrops jacaraca* and *Naja naja atra*. A large number of experiments and the results are given in detail; these can only be summarized here. Readers desiring more should consult the original, in which the many points are clearly set out.

Immunization was carried out by injections of a mixed venom and antivenene, and by venom-antivenene precipitates, and with toxoid. The degree and duration of immunity produced are estimated and protocols of the results are presented. The following summarizes the main results :—

I.—As regards immunization against the Lachesis venom :—

1. Injection of the venom-antivenene mixture gave rise to immunity, but not of high degree.
2. The effect of using the precipitates was greatest after intraperitoneal injection, and then, in order, intramuscular, intravenous and subcutaneous.
3. Subcutaneous injection with toxoids produced high immunity in animals. The degree was greater 10 days after the final inoculation than after 3 days, particularly if the sediment was also injected. The effectiveness was practically the same after 14 weeks' incubation as after 6 weeks'; it is, therefore, wiser to employ the former for immunizing human beings. Immunity is maintained for several weeks, and the antigenicity of the toxoid is not impaired by heating to 60°C. for 30 minutes on 3 successive days.
4. Immunization of rabbits by cutaneous application of an ointment of the venom in lanolin to the shaven skin was high and persisted for 1–2 months.
5. Reimmunization by subcutaneous injection of toxoid was obtained more rapidly than the primary immunization.

II.—Active immunization against Cobra venom :—

1. Active immunization with increasing doses of venom must be carried out slowly and with caution.
2. The use of precipitates does procure immunity, but not very marked.
3. The toxoid, which was found to be no longer toxic after being kept for 6 weeks at 40°C., was apparently ineffective for mice and gave poor results in rabbits. This may be, in part, accounted for by the fact that the venom was denatured and had lost to some degree its antigenicity before it was used for preparation of toxoid.

Lastly, as regard precipitation of venoms by antivenenes; this was observed to be specific among Colubrines and Viperines; the antivenene potency and the precipitin titre of antisera might not run parallel, and the correlation between flocculation and neutralization of venom and antivenene *in vitro* differed both with the kind of venom and the animal employed for production of the antiserum.

H. H. S.

VON KLOBUSITZKY (D.). Biochemische Studien ueber die Gifte der Schlangengattung Bothrops. II. Mitteilung. Eine verbesserte Methode zur Herstellung von Bothropotoxin. [**An Improved Method of Preparation of Bothropotoxin.**]—*Arch. f. Experim. Path. u. Pharm.* 1936. Mar. 18. Vol. 180. No. 5/6. pp. 479–481.

The methods described by the author [this *Bulletin*, 1936, Vol. 33, p. 380], had the drawback that they produced only a small and variable amount of bothropotoxin, and the latter, besides having a toxic property, was also coagulative. For the new method, which is described at length, it is claimed that it yields a larger amount

of bothropotoxin and this has much stronger neurotoxic properties and much diminished coagulative power. The bothropotoxin so obtained is free from nitrogen, hydrogen, phosphorus and iron. Whereas the venom, from which it is prepared, has a minimum lethal dose of 0·26–0·27 mgm., that of the bothropotoxin is 0·055–0·060 mgm. A m.l.d of the original venom coagulates 5 cc. of oxalated horse blood in 4 minutes; that of bothropotoxin only does so in 20 minutes.

H. J. Walton.

v. Klobusitzky (D.) & König (P.). Ueber die Bindung des Bothropotoxin durch Schlangensera. [**The Union of Snake Venoms with Antivenenes.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1936. Feb. 18. Vol. 87. No. 3/4. pp. 202–212. [18 refs.]

—— & ——. Ueber die Bindung des Bothropotoxin durch Schlangensera. II. Mitteilung. Bindung durch Buschmeister- (Lachesis muta-) Serum.—*Ibid.* pp. 330–334.

None of the animal poisons which have been isolated in a more or less pure state, bee-venom, ophiotoxin, crotalotoxin, scorpion venom and others, has been tested as regards its immunological properties. Are these nitrogen-free poisons to be regarded as true toxins, with power to produce antigens, and to enter into specific combination with the homologous antibodies?

The authors have isolated, in a nearly pure state, the toxic substance of a Brazilian viper, *Bothrops jararaca*. They have succeeded in preparing the active principle of this in a nitrogen-free condition and with a constant degree of toxicity. This bothropotoxin is a typical poison of the central nervous system, and causes death in pigeons within a few minutes by paralysis of the respiratory centre. Besides this neurotoxic property, bothropotoxin exerts a coagulative effect, though in a much less degree than the crude venom; this is probably to be attributed to an impurity, which it has not hitherto been found possible to remove.

The experiments were carried out as follows:—

A 0·1 per cent. solution of bothropotoxin was made: the minimum lethal dose (m.l.d.) of this was 0·6 cc., or 0·06 mgm. The experiments were conducted both *in vitro* and *in vivo*; in the former, a definite quantity of the bothropotoxin solution was mixed with different quantities of the snake antiserum, and the mixture, after standing for half an hour, injected into the wing-vein of pigeons. In the experiments *in vivo*, the bird was given a lethal dose of the toxin, and, as soon as the second stage of poisoning occurred, when the pigeon fell on its back, the *Bothrops* serum was given: this procedure is called by the authors, Type I. In Type II, the serum was given immediately after the toxin. In both types the serum was administered subcutaneously or intramuscularly. In the experiments with rattlesnake serum, besides the two types described above, a third set was carried out in which the serum and bothropotoxin solution were mixed together in the syringe, or else the serum was injected into the vein of one wing, and the bothropotoxin immediately afterwards into the vein of the other wing.

The experiments with *Elaps* serum were only carried out *in vitro*, and all gave a negative result.

The titres of the sera were found to be as follows :—

One cc. of monovalent *Bothrops* sera neutralized 3·8, 2·4, or 2·2 mgm. of crude venom of *B. jararaca.*

One cc. of rattlesnake serum neutralized 0·9 mgm. of the venom of the South American *Crotalus terrificus terrificus.*

One cc. of the bivalent *Elaps* sera neutralized 0·15 mgm. of the venom of *Micrurus corallinus,* and 0·25 mgm. of *Micrurus frontalis.*

The m.l.d. of dried *B. jararaca* venom is from 0·02 to 0·022 mgm., but the toxicity diminishes with time, and the m.l.d. may be as much as 0·6 mgm.; the loss of toxicity is probably due to oxidation. The venom used in the production of the bothropotoxin used in these experiments had a m.l.d. of 0·26–0·27 mgm. Since the m.l.d. of bothropotoxin is 0·06, this is about four to four and a-half times as potent as the former, but only one-tenth of the potency of the fresh venom. It was found that the toxic element of the venom only represented about one-third of the dried substance, so that the m.l.d. of fresh crude venom is really 0·007 mgm., and of that used for the production of bothropotoxin, 0·09 mgm. This last figure indicates what the m.l.d. of bothropotoxin should be theoretically; actually it is about one-third less, namely 0·06 mgm. The cause of the discrepancy will be discussed in a later communication; all that can be said now is that an early symptom is vomiting, which does not occur in poisoning with bothropotoxin.

In the experiments, both *in vitro* and *in vivo,* it was found that bothropotoxin combined with and neutralized its homologous serum just as whole venom does. When bothropotoxin and its antiserum were given, the result depended upon whether the amount of bothropotoxin was sufficiently in excess of that required to neutralize and combine with the serum to give the m.l.d.

In the rattlesnake experiments it was found that 1 cc. of rattlesnake serum neutralized 1·2 mgm. of the toxin of the corresponding snake, and 0·02 mgm. of that of *Bothrops jararaca*; that is, the rattlesnake serum was ten times as active in the former case. The experiments showed that rattlesnake serum, both *in vitro* and *in vivo* (only when given intravenously in the latter case), neutralized the same amount of bothropotoxin as *Bothrops* serum. The authors consider that this fact indicates that there is a close chemical relationship between the toxin of rattlesnake venom and bothropotoxin. There are several points of resemblance between the two; for instance, both are neurotoxic; again, when very large doses are given, the effect of bothropotoxin is more like that of rattlesnake venom than that of the whole venom of *Bothrops*; if 10–15 times the m.l.d. is given, *B. jararaca* venom causes death in a few seconds, that of *Crotalus terrificus terrificus* in 10–15 minutes, while bothropotoxin stands in an intermediate position, causing death in 3 minutes.

The authors summarize their results as follows :—

1. *Bothrops* serum neutralizes bothropotoxin both *in vitro* and *in vivo* in a definite proportion.

2. The South American rattlesnake serum also neutralizes bothropotoxin *in vitro* in a definite proportion.

3. The same serum neutralizes bothropotoxin in a definite proportion *in vivo* only when given intravenously.

4. *Elaps* serum has no combining and neutralizing power with bothropotoxin.

5. It is probable that there is a close chemical relationship between bothropotoxin and the neurotoxic substance of rattlesnake venom.

H. J. Walton.

VON KLOBUSITZKY (D.) & KÖNIG (P.). Biochemische Studien ueber die Gifte der Schlangengattung Bothrops. III. Mitteilung: Die Trennung der gerinnungsfördernden Substanz von dem Bothropotoxin und den uebrigen Sekretbestandteilen. [**The Isolation of the Coagulating Substance of Bothropotoxin from the Other Constituents of the Venom.**]—*Arch. f. Experim. Path. u. Pharm.* 1936. May 25. Vol. 181. No. 3. pp. 387–398. [18 refs.]

In a previous paper the authors described a substance, bothropotoxin which they have obtained from the venom of *Bothrops jararaca* (= *Lachesis lanceolatus*): it possesses neurotoxic and coagulating, but no haemolytic, properties. Earlier attempts to separate the coagulating from the toxic principle failed; they now describe the method by which they have succeeded in effecting this.

By suitable fractionization by means of ammonium sulphate, and subsequent dialysis under pressure for a period of eight days, a colourless solution was obtained, which gave a dry residue of from 0·30 to 0·34 per cent. When used in quantity equivalent to ten times the lethal dose (measured as dried residue) of the stock solution, it caused no symptoms in pigeons, but was a very active coagulant. This globulin fraction was treated with basic lead acetate to precipitate albumen, the precipitate removed by centrifuge, and the solution dialysed until free from lead; it was then concentrated by ultrafiltration to one-third of its original volume.

The chemical composition of the coagulating substance is not known. It cannot be said whether it is an albumen-derivative, or even whether it is free from nitrogen, as it has only been obtained in dilute solution, and mixed with a small amount of albumen; it is probable that it is an enzyme, a form of coagulase.

The authors suggest that its use should be tested in cases of severe haemorrhage and haemophilic conditions, and they offer to supply samples for this purpose. *H. J. Walton.*

VON KLOBUSITZKY (D.) & KÖNIG (P.). Biochemische Studien ueber die Gifte der Schlangengattung Bothrops. IV. Mitteilung: Die Wirkung der gerinnungsfördernden Substanz in vivo. [**Biochemical Studies of the Venom of** *Bothrops*. **The Action of the Coagulating Principle** *in vivo*.]—*Arch. f. Experim. Path. u. Pharm.* 1936. Sept. 30. Vol. 182. No. 5. pp. 577–583. [16 refs.]

The authors refer to the work of HOUSSAY and SORDELLI (1919), who studied the changes in the coagulability of the blood in dogs and rabbits after intravenous and subcutaneous injection of snake venoms. They found that large doses (2 mgm. per 10 kgm. dog) quickly produced intravascular coagulation; with smaller doses (1 mgm. per 10 kgm. dog), after a temporary shortening of the coagulation time (positive phase), the fibrinogen is precipitated and the blood remains uncoagulable (negative phase).

The authors consider that, in these experiments, too large doses were given, and the times of observation were too short, for it to be

possible to draw any useful conclusions as regards the therapeutic use of the venom; they have therefore carried out experiments on pigeons with the coagulating substance isolated by them from the venom of *Bothrops jararaca.*

They had found previously that a solution of this substance, if entirely free from albumen, and salts, loses its activity very quickly, and so they used a solution containing 0·042 per cent. of dried matter, of which 0·0150 per cent. consisted of albumen. The strength of the solution was such that 1 cc. completely coagulated 5 cc. of oxalated blood of the horse in three minutes. Two series of experiments were made: in the first series blood was withdrawn and tested for coagulability 1 minute and 20 minutes after the injection; in the second series, after 20 minutes and 24 hours. The coagulating solution was used at different degrees of strength.

It was found that the result depended upon the time that had elapsed after the injection. Large doses diminish the coagulability at first; after 24 hours, the coagulability is increased. Small doses have no decided effect at first; but after 20 minutes they accelerate coagulation, and this result persists for at least 24 hours.

The authors estimate that in a pigeon weighing 350 gm. the volume of blood is 20 cc., and that the coagulating constituent of the venom is active in a dilution of 0·00000055 mgm. per cc. of the pigeon's blood. On the strength of these experiments on pigeons, and assuming that the total amount of blood in a man is 4·5 litres, they think that 0·0025 mgm. should be a suitable dose for therapeutic use in cases of haemorrhage and haemophilia. *H. J. Walton.*

v. Klobusitzky (D.) & König (P.). Ueber die Bindung der gerinnungsfördernden Substanz des Giftes der *Bothrops jararaca* durch Schlangensera. [**Neutralization of the Coagulating Substance of *Bothrops jararaca* Poison by Snake Sera.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1936. Nov. 3. Vol. 89. No. 3/4. pp. 145–160. [17 refs.]

The question whether the coagulant action of the Bothrops poison is caused by a specific substance or by the neurotoxic component may be considered settled in favour of there being two different component substances. It is not altogether clear, however, whether the neutralizing power of the antisera to snake poisons is strictly specific. As the authors had succeeded in separating from the crude poison of *Bothrops jararaca* a coagulating substance, it seemed worth while testing it for its serum specificity. It may be explained that the bushmaster (*Lachesis mutata*) and S. American rattlesnake (*Crotalus terrificus*) antisera combine quite non-specifically with the purified neurotoxic component of the Bothrops poison and, yet, the *crude* Bothrops poison is only neutralized by rattlesnake antisera to a very slight extent. The problem, therefore, to be solved was whether the neutralization of the purified coagulating substance was specific or, like the purified neurotoxin also, non-specific.

The coagulant substance was available in the form of very dilute, completely protein and biuret-free solutions obtained from the crude poison of *Bothrops jararaca* (former name *Lachesis lanceolatus*). Neutralization experiments were carried out with monovalent Bothrops-, rattlesnake-, and bushmaster-sera and with divalent coral snake-sera (*Micrurus frontalis* and *M. corallinus*).

The results of these tests may be summarized :—(1) Coagulating substance from *Bothrops jararaca* poison is neutralized equally by *jararaca* and bushmaster antisera. (2) The bivalent coral antisera and rattlesnake antisera have no combining action with this Bothrops coagulating substance. (3) The previous work on the immunological, and perhaps also chemical, identity of coagulating and neurotoxic substances may be combined, with the work now carried out, in the following table :—

Neurotoxic Substances		Coagulating Components.	
Identical with Bothrops toxin	Not identical with Bothrops toxin	Identical	Not identical
B. jararaca *Lachesis mutata* *Crotalus terrificus*	*Micrurus frontalis* *M. corallinus*	*B. jararaca* *L. mutata*	*C. terrificus* *M. corallinus*

W. F. Harvey.

HANUT (Charles Joseph). La coagulation *in vitro* du plasma par les venins des *Bothrops* dépendelle uniquement d'une action thrombinique ? [**Is Coagulation *in vitro* of Plasma by Bothrops Venom due solely to Thrombin ?**]—*C. R. Soc. Biol.* 1936. Vol. 122. No. 22. pp. 796–798.

That Bothrops venom in quite small doses will coagulate the oxalated plasma of the rabbit and solution of fibrinogen is known and has been shown to be due to thrombin action ; but this may not be the only cause. The author examined for the presence of proserozyme by the method of adsorption with tricalcium phosphate, but found this unsuitable because the thrombin of the venom was strongly adsorbed by this substance. He therefore carried out the following procedure, using the venom of *B. atrox* :—

To 4 cc. of clear oxalated rabbit plasma are added 12 cc. physiological saline and 4 cc. of a 1 in 20 million dilution of the venom in saline. The mixture is placed in an incubator at 37°C. A clot forms in about an hour which on defibrination yields a clear liquid. This is returned to the incubator and a fresh clotting occurs. This procedure is repeated until the fluid obtained no longer clots, *i.e.*, the total duration in the incubator is 4 hours. In Pyrex tubes, 12 mm. diameter, are placed 0·4 cc. of the liquid so obtained and 0·35 cc. of physiological saline containing 1·05 gm. $CaCl_2$. After varying intervals 2 drops of a suspension of cytozyme and 3 minutes later 0·2 cc. of dioxalated plasma (as solution of fibrinogen) are added.

Coagulation after 30 seconds' to 2 minutes' contact is due to the venom thrombin. But " if the liquid contains only thrombin, after longer contact of 5 minutes or more the mixture ought still to coagulate in about 6 minutes ; but it clots in a much shorter time, 2 mins. 7 secs. to 3 mins. 22 secs. This can hardly be explained in any other way than by admitting that in the defibrination liquid there exists a proserozyme which, in the presence of calcium, is transformed into serozyme after an interval of 2–5 minutes." This is analogous to what occurs with a staphylocoagulase. The proserozyme was found similarly in the venom of *B. neuwiedi* and *B. alternata*, but not in that of *B. nummifera*.

H. H. S.

Link (Th.). Der Einfluss der Schlangengifte auf die Blutgerinnung. 2. Mitteilung. *Crotalus terrificus, Bothrops jararacussu.* [**The Action of Snake Poison on Coagulation of Blood.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1937. May 27. Vol. 90. No. 4. pp. 352–357.

Following up his investigations on Crotalus venom the author has studied the action of the venom of *Crotalus terrificus* in inhibiting blood-clotting. He finds that this is brought about when large doses are used and is due to destruction of fibrinogen. In small doses, on the contrary, coagulation is promoted and is best demonstrated by adding oxalated blood to the venom. He tested in a similar way the venom of another South American snake, *Bothrops jararacussu*, and found it to act in the same way—large doses inhibiting, small promoting, clotting. Both factors in the case of the Bothrops are neutralized by the antivenene. If the venom of *B. jararacussu* is heated to 70°C. for a quarter of an hour, the thermostable inhibiting constituent can be separated from the thermolabile coagulant factor, but compared with the unheated venom the toxicity is reduced to one-tenth. *H. H. S.*

Vellard (Jehan). Variations géographiques du venin de *Bothrops atrox* L. [**Geographical Variations in the Venom of** *Bothrops atrox.*]—*C. R. Acad. Sci.* 1937. May 3. Vol. 204. No. 18. pp. 1369–1371.

Variations in venom potency are of three kinds: individual, seasonal and geographical. The author in this paper deals only with the last. He chose *Bothrops atrox* because of its wide distribution and compared the venom from specimens in Venezuela, Martinique, Northern Brazil and Costa Rica.

The Venezuelan strains were distinguished by their coagulant and haemolytic properties, whereas the proteolytic, anti-complementary and anticoagulant actions were weak. *In vivo*, their toxicity was great, but the haemorrhagic oedema produced did not as a rule go on to necrosis.

Martinique strains (*fer de lance*) were nearly equal to those of Brazil in proteolytic power, but their coagulant action was small, and haemolytic a little below that of the Venezuelan strains. *In vivo*, they evince a marked neurotropic action and severe local necrosis.

That of Costa Rica has but slight proteolytic and haemolytic action; its coagulant and toxic effects approximate those of the Venezuelan strains. *In vivo* extensive haemorrhagic oedema is seen, but seldom necrosis.

The above findings indicate the advisability of preparing antivenenes peculiar to the country in which they are likely to be needed.

H. H. S.

Nagamitu (Gun'itirô). Experimentelle Untersuchung ueber das Ancistrotongift [**Study of the Venom of Ancistrodon.**]—*Okayama-Igakkai-Zasshi* (*Mitt. d. Med. Gesellsch. z. Okayama*). 1936. July. Vol. 48. No. 7. [In Japanese pp. 1650–1657. With 6 charts. German summary p. 1650.]

The venom of *Ancistrodon blomhoffii* was investigated. Its chief action on the rabbit was to depress the respiratory centre, and death

was due to paralysis of this centre. Its nerve action was tested on the frog. It did not affect the nerves or motor-end plates, nor the skeletal muscles ; no evidence was obtained of any haemolytic action.

H. H. S.

Tomoyama (Kazuo). **On the Influence of Formosan Principal Snake Venoms upon the Rate of Sedimentation of the Erythrocytes of Normal Rabbits.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1936. Aug. Vol. 35. No. 8 (377). [In Japanese pp. 1627–1644. [33 refs.]. English summary pp. 1644–1645.]

The venoms investigated were those of *Ancistrodon acutus*, *Trimeresurus macrosquamatus*, *T. gramineus*, *Naja naja atra* and *Bungarus multicinctus*. The venoms were injected into the marginal ear vein of healthy adult rabbits, 15 male and 25 female [dose of venom injected is not stated] and the sedimentation rate determined 5 minutes before and half an hour, one hour, one and a half and two hours afterwards. In the tables readings are given after 1, 2, 3, and 24 hours, so only general conclusions can be stated :—

1. Individual animals differed from one another, but this seemed to bear no relation to sex. [According to the tables the minima were lower and the maxima higher in females than in males, but the averages were lower in the females.]
2. The haemorrhagic venoms of *A. acutus* and *T. macrosquamatus* caused slowing of the sedimentation rate after half and one hour, but at 1½ and 2 hours there was acceleration. That of *T. gramineus* caused retardation between ½ and 2 hours.
3. The neurotropic venoms of *N. naja* and *B. multicinctus* were followed by slight degree of acceleration at 1½ and 2 hours, no difference from the normal being observed at the shorter periods of ½ and 1 hour.
4. The haemorrhagic and neurotropic venoms could be differentiated by the sedimentation rates after ½ and 1 hour.
5. The retardation or acceleration of the rate appears to be closely connected with increase or decrease in the total number of erythrocytes.

H. H. S.

Oh (Jintetsu). Ueber die Wirkung des Giftes gewisser formosanischer Schlangen auf das Schmerzzentrum. [**The Action of Certain Formosan Snake Venoms on the Pain Centre.**]—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1936. Sept. Vol. 35. No. 9 (378). [In Japanese pp. 2083–2090. [18 refs.] German summary pp. 2090–2091.]

The author's experiments aimed at determining whether certain snake venoms affected the pain centre and, if so, in what doses they acted. Okushima's method was employed, the venoms being dried over sulphuric acid and then dissolved in physiological saline. The venom was injected subcutaneously in the back of mice and the pain response tested by a needle-prick in the tail. The following venoms were tested : *Trimeresurus macrosquamatus*, *T. gramineus*, *Ancistrodon acutus*, *Naja naja atra* and *Bungarus multicinctus*.

The venoms of the Trimeresurus species in a dose of 0·001 mgm. per gm. body weight had no effect on the pain centre, but in doses of 0·005 mgm. susceptibility to pain was impeded, whereas that of *Ancistrodon acutus*, even up to 0·01 mgm. (the minimum lethal dose) had no effect.

Of the Elapinae ; the venom of *Naja atra* in doses of 0·00001 mgm. per gm. very slightly reduced susceptibility to pain ; with 0·00005 mgm. it was quite obvious and with twice this dose very marked and even more with 0·0005 mgm., the minimum lethal dose. With that of *Bungarus multicinctus*, 0·00001 mgm. had a slight action, 0·00005 very distinct and the effect was more and more marked up to the m.l.d. of 0·0003 mgm.

Briefly, the Elapine venoms had a definite and fairly rapid action in reducing susceptibility, whereas the Crotaline had little or none even when the dose approached the corresponding minimum lethal dose.

H. H. S.

Oh (Jintetsu). Ueber die Wirkung des Giftes gewisser formosanischer Schlangen auf die motorischen und sensiblen peripheren Nerven. [**The Action of Certain Formosan Snake Venoms on the Motor and Sensory Nerve-Endings.**]—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1936. Sept. Vol. 35. No. 9 (378). [In Japanese pp. 2092–2099. [16 refs.] German summary pp. 2099–2100.]

The same venoms as above were tested by the Santesson-Osaki method, with the frog as the experimental animal, the venom being dried and then dissolved in Ringer's fluid.

It was found that the Crotaline poisons, those of *T. mucrosquamatus*, *T. gramineus*, and *A. acutus*, paralyse the sensory nerves much more rapidly than the motor, and that of *T. gramineus* was the most potent, *T. mucrosquamatus* next, and *Ancistrodon acutus* the least. The venoms of the Elapine snakes, *M. n. atra* and *B. multicinctus* act on both sensory and motor endings, paralysing them fairly quickly ; that of *Bungarus* was more potent than that of *Naja* and both were more active in this respect than any of the Crotalines. *H. H. S.*

Barros (Evandro Fonseca). Contribuição ao conhecimento da hyper-sensibilidade ao veneno ophidico. [**Hypersensitivity to Snake Poison.**]—*Brasil-Medico.* 1936. Mar. 21. Vol. 50. No. 12. pp. 243–246. English summary.

The author refers to previously recorded cases, one of which, for example, was evidenced by a generalized dermatitis, the patient having been bitten by a rattlesnake on a former occasion. He records two more in this article. Both had been in the habit of handling snake-venom, in dried or liquid form, for about two years. The first was actually bitten by a rattlesnake when he was trying to extract its venom, the second was not bitten but the symptoms of hyper-sensitivity were similar in both. These symptoms were violent sneezing when handling the venom, or even coming near it (one sneezed 75 times in succession), followed by thirst and sweating ; there might be rhinorrhoea, dyspnoea, cough and a considerable amount of expectoration. These lasted for 1–2 days at first, but later might persist for 5 days after a single exposure, such as a vial being opened in their presence. They became so sensitive that an attack would come on if they entered a room in which a vial had been opened, or through which it had been taken, two hours before. Attempts at

desensitization by application of very dilute solutions of the venom to the nasal mucosa have proved unavailing.

Two others working in the author's laboratory are now showing signs of sensitivity—an attack of sneezing and rhinorrhoea when standing for some time near an open vial. *H. H. S.*

SEILER (Johannes). Versuche zur Schmerzbekämpfung mit Kobragift. [**Cobra Venom as an Analgesic.**]—*Muench. Med. Woch.* 1936. Mar. 27. Vol. 83. No. 13. pp. 527–528.

The author sought to confirm or refute some results reported lately from the Calmette Institute. (He gives the following references to papers describing them:—*C. r. Acad. Sci.*, Vol. 197, No. 3 of 17/7/33; MONAELESSER and TAGUET, *Bull. Acad. Méd.*, Vol. 109, No. 11, séance du 14/3/33; PITON, *Presse Méd.*, 1934, No. 2).

In these papers it was stated that:—

1. In experimental carcinoma of mice, injections of cobra venom caused involution in some of these animals.

2. Cobra venom appeared to have an inhibitive action on tissue cultures.

3. The author quotes CALMETTE's personal experience of an accidental bite of a cobra, which caused extensive anaesthesia which only disappeared after antivenene treatment.

4. MONAELESSER found that cobra venom stopped the painful neuralgias of lepers.

5. MONAELESSER and TAGUET tried the effect of the venom on 115 cancerous patients with favourable results. They believe that, besides a decided diminution of the pain, there was in certain cases improvement in the condition of the tumour, and decrease in the cachexia. ORTICONI and RAVINA report that "inoperable" cases often improved and became fit for operation. But, in general, diminution of pain was the most important result of the treatment.

The author used a solution of dried cobra venom in physiological salt solution. In healthy people he found that, although the actual injection caused no appreciable pain, a painful induration occurred at the seat of injection. He tested the treatment on a patient with very severe sciatica, on another with pain in the leg due to arterio-sclerosis, on two patients with bronchial carcinoma and pain in the arms, and on a man with carcinoma of the prostate and pain in the leg. The patients all had some initial pain following the injection; in some cases this was severe and it usually lasted for 24 hours. After one injection, two patients refused further treatment on this account; two others, who had each received four injections, had more and more pain after each injection, and the treatment had to be abandoned. The only patient who had no increase of pain was the one with arteriosclerotic pains in the leg; in his case a sudden arterial block necessitated amputation.

The author's results entirely failed to confirm the French reports, and he is unable to explain the lack of agreement. He suggests that possibly the cobra venom used was not pure, and may have contained some organic extract, as described in PITON's paper.

H. J. Walton.

KIRSCHEN (Martin). Ueber das Kobratoxin und seine therapeutische Verwendung. [**The Therapeutic Uses of Cobra Venom.**]—*Wien. Klin. Woch.* 1936. May 22. Vol. 49. No. 21. pp. 648–651.

The author refers to the results obtained by MONAELESSER and TAGUET, SAENCE and COSTIL, who found that cobra venom had a curative effect on both transplanted and spontaneous carcinoma in mice, and that one-tenth of the minimal lethal dose injected into the tumour of the mouse caused it to disappear permanently. Other observers (LAIGNEL-LAVASTINE, PASQUALINI, MUFFRE, BOER and others) reported improvement in the condition of inoperable carcinomas in human subjects, or, at least, improvement in their general condition.

These results induced the author to try the effect of cobra venom on painful cases of inoperable and recurrent carcinoma; he also tested the anodyne effect of the treatment on cases of neuralgia and neuritis. He used a colloidal solution of standardized venom, free from bacteria, haemorrhagin and haemolysin, supplied by the Dumatras laboratory of Paris.

The optimum for each patient must be found by experiment. He began with small doses, given subcutaneously in the upper part of the back or in the gluteal region, repeated at intervals of three days; he did not try injections directly into or in the neighbourhood of the tumours. If the dose was too small, there was little, or only a temporary effect; if too high, there was increase of pain and general symptoms. Often, with small doses, the pain diminished and the patient felt better; in such cases the same dose was continued, and the intervals between the injections lengthened. If no result followed after four or five injections, the dose was increased.

The author treated 23 cases; of these 15 were patients with cancer of the stomach, 3 of the lungs, 3 of the intestines, and 2 of the mammary gland.

Of the 10 cases of inoperable cancer of the stomach, five were unaffected by the treatment; in three other cases, there was a decided temporary improvement. Thus, a man aged 60, after three weeks' treatment had lost all pain, and gained 7 kilograms in weight; the blood, which showed marked anaemia at first, improved very much. The improvement lasted for two years, after which the man began to lose weight, and his condition deteriorated.

A woman aged 57, with inoperable carcinoma of the stomach, began treatment in October 1933. She improved rapidly, gained 6 kilos in weight, lost all pain, and feels well now. Another man, aged 64 years, improved considerably for 6 months, had no more pain, and gained weight; after that he had a relapse and died. Two other patients improved, lost pain, gained weight, and continued for some time to feel well. In five patients with gastric carcinoma, who had undergone operation, cobra toxin caused diminution of pain in four, and a very decided temporary improvement in the fifth. Two cases of bronchial carcinoma were unaffected by the treatment; the third case was favourably influenced as regards pain.

The results in three cases of intestinal cancer were good; pain and tenesmus were much lessened; in one case, very decided improvement lasted for a year.

In two cases of mammary carcinoma, with metastatic growths after operation, the pain was much diminished; the patients, however,

were undergoing intensive X-ray treatment at the same time as the injections, and it is impossible to say to which treatment the favourable result was due. The author draws the following conclusions :—

Cobra toxin appears to have no specific effect on carcinoma in man. In his series of cases there was no real cure, and no disappearance or even diminution in size of the tumour, such as French observers have reported, and such as might be expected from experiments on animals. There is no doubt that cobra venom is a strong analgesic, which can replace morphia. At present it is impossible to say to which constituent of the venom this effect is to be attributed. The decided analgesic effect is of great importance, for the venom acts efficiently in the case of the usually cachectic and undernourished patients, without, as morphia does, destroying their appetite and weakening their defensive resistance to the disease.

The price of the original preparation is high, but recently a satisfactory and cheaper one has been produced at the Vienna Serotherapeutic Institute.

Lately the author has used cobra venom treatment for patients with neuralgia and neuritis of varied origin, and he has observed a well-marked analgesic effect. Seven cases, of which two were of severe sciatica, were quickly relieved of pain. *H. J. Walton.*

Kirschen (Martin). Ueber das Kobratoxin und seine therapeutische Verwendung. [**The Therapeutic Application of Cobra Venom.**]—*Mitt. d. Volksgsndhtsamtes.* 1936. Dec. 1. No. 12. pp. 313-316.

The analgesic properties of cobra venom are becoming widely known. The author refers to 23 cases of carcinoma and several of severe neuralgia so treated, many with good effect. Among the former were 15 of carcinoma of the stomach, 10 of them in an inoperable stage. Three of the last are detailed ; they lost the pain and appetite improved. Of the other seven, two showed distinct improvement, losing pain, gaining weight and feeling generally better, five remained unaffected. In those operated upon, the pain was much lessened. Other cases included 3 of malignant disease of the lungs, 3 of the rectum and 2 of the breast. The rectal cases showed great relief of the tenesmus as well as of pain.

Of the non-malignant patients 7 suffered from severe sciatica and relief was obtained " in a relatively short time." The dose to be given varies and the optimum has to be determined for each patient [see previous summary and also this *Bulletin*, 1936, Vol. 33, p. 396]. *H. H. S.*

Roldán (Amalio). La venenoterapia en el cancer. Sus fundamentos y aplicaciones actuales. [**The Effect of Snake Venoms in Cancer.**] —*Bol. Asoc. Med. de Puerto Rico.* 1936. Feb. Vol. 28. No. 2. pp. 32–36.

Among remarks of a general nature concerning snake bite and venoms the following are of special interest to readers of this *Bulletin*. The use of cobra venom in a strength of 1 in 80,000 in 8 cases to relieve the pain of cancer of the throat, involving pharynx and larynx, which, as is well known, is one of the most painful sites of the carcinoma, was followed by marked relief of the pain in six of them ; in one no change was observed, while in the last " not only did the pain cease, but the tumour disappeared completely." Dr. Korbler of Zagreb

employed Poskok venom (*Vipera ammodytes*) in doses of 5–10 rat units in 26 cancer cases; the pain was relieved in all and in some modification in the growth was observed. It seemed also to bring about improvement in the general state. The same venom was used with success in the relief of pain due to neuralgia, to rheumatism and arthritis deformans [see also this *Bulletin*, 1936, Vol. 33, p. 396.]

H. H. S.

Brünner-Ornstein (Martha). Behandlungsversuche mit Kobratoxin bei neurologischen Erkrankungen. [**Cobra Venom in the Treatment of Neurological Affections.**]—*Wien. Klin. Woch.* 1937. Jan. 29. Vol. 50. No. 4. pp. 127–128.

The author employs two strengths of the venom, one used in an initial dose of 0·0001 cc. standardized to 4 mouse-units, the other 0·0005 cc. or 20 mouse-units per cc. One cc. of the former contains 0·1 mgm. of the cobra venom. He records very gratifying results in cases of obstinate trigeminal neuralgia, relief being speedily attained (perhaps in half an hour). Of fourteen cases of very severe neuralgia six have been free of pain for 3–4 months, four are distinctly better. The author tried Crotalus venom in some cases, and though benefit resulted, it was less marked than with cobra venom. Good effects have been obtained in rheumatic conditions and the author proposes to try the treatment in other cases of neuralgia and neuritis and also for the pains of tabetic crises. [Dr. Burgess Barnett in a personal communication to the reviewer states that he has obtained excellent results in a case of tabes, the crises having ceased for 8 months.]

H. H. S.

Finkelman (Isidore). **Snake Venom (Moccasin) in the Treatment of Epilepsy.**—*Jl. Lab. & Clin. Med.* 1937. Mar. Vol. 22. No. 6. pp. 572–575. [12 refs.]

The idea of employing snake venom for treatment of epilepsy arose from an alleged freedom from attacks in epileptics after they had been bitten by snakes. Splangler used Ancistrodon venom and reported favourable results, explaining them by the decreased rate of coagulation caused by the venoms. Later, he seems to have abandoned this theory but found the treatment useful in those who reacted by an eosinophilia. Contradictory reports thereafter appeared, and the author has tried it on eight epileptics; he used Moccasin-Mulford venom 1 : 3,000, starting with 0·2 cc. intradermally and increasing twice weekly by 0·2 cc. to a maximum dose of 1·0 cc., and then at weekly intervals.

The patients' records were carefully studied as to previous frequency of convulsions both under luminal and without treatment. Use of venom alone was followed by increase in frequency and severity of convulsions and luminal had to be re-started. The patients became also more irritable. The author concludes that at all events in institutional epileptics (who show mental deterioration and usually have organic brain changes more marked than extramural cases) venom therapy not only does not render them refractory, but, also on the contrary, rather more susceptible to convulsive seizures.

H. H. S.

v. Klobusitzky (D.). Schlangengifte in der Therapie. [**Therapeutic Uses of Snake Venom.**]—*Klin. Woch.* 1937. Apr. 17. Vol. 16. No. 16. pp. 569–575. [87 refs.]

This article is brought to the notice of readers because it comprises an excellent summary of a difficult subject—the various uses to which different snake venoms have been put in the treatment of disease. Being itself a summary, it cannot be abstracted ; it should be read by all interested. Venoms of many species are dealt with, Colubrines, Crotalines, Viperines and their employment in malignant tumour patients, in neuralgia, rheumatic conditions, epilepsy, haemorrhagic diseases and others. A large number of references is appended, the ample documentation greatly facilitating further study. *H. H. S.*

Eagle (Harry). **The Coagulation of Blood by Snake Venoms and its Physiologic Significance.**—*Jl. Experim. Med.* 1937. May 1. Vol. 65. No. 5. pp. 613–639. With 5 figs. [23 refs.]

This article treats the subject of snake venoms and their haemostatic action from the physiological aspect, but as the empiric use of these venoms in clinical practice is becoming more extensive this empiricism must give way before the scientific determination of their mode of action. The physiological determination is essential to their rational employment, hence the value of this article. The following were the venoms tested : *Ancistrodon piscivorus, Bitis arietans, Bothrops atrox, B. jararaca, B. nummifera, Crotalus adamanteus, C. atrox, C. horridus, C. terrificus basiliscus, C. terrificus terrificus, Micrurus* mixed, *Naia flava, N. naia, Notechis scutatus. Scpedon haemachates, Vipera ammodytes* and *V. russelli.*

The results are summarized in the author's words as follows :—

" Nine of the 17 venoms here tested were found capable of coagulating citrated blood or plasma. As has been believed by most workers in the field, 7 of these 9 coagulant venoms convert fibrinogen to an insoluble modification resembling fibrin (*Bothrops atrox, Bothrops jararaca, Bothrops nummifera, Crotalus adamanteus, Crotalus horridus, Crotalus terrificus basiliscus, Crotalus terrificus terrificus*). The optimum pH for this coagulation was determined for 3 of these, and was found in each case to be approximately pH 6·5, the same as that for the action of thrombin on fibrinogen. Unlike thrombin, however, the fibrinogen-coagulating activity of the venoms was unaffected by the antithrombin elaborated in the course of anaphylactic shock.

" In addition to coagulating fibrinogen directly, 3 of these venoms (*Bothrops atrox, Bothrops jararaca,* and to a less extent, *Crotalus terrificus basiliscus*) acted on prothrombin to convert it to thrombin, without the necessary intervention of either calcium or platelets. Finally, 2 venoms (*Notechis scutatus,* and to a slight extent, a mixed *Micrurus* venom), which had no demonstrable effect on purified fibrinogen, nevertheless converted prothrombin to thrombin.

" Unlike the reaction between the venoms and fibrinogen, this activation of prothrombin has no definite pH optimum, but takes place over a wide zone (pH 5·6–8·3). In the case of *Bothrops atrox,* there was some indication that the initial velocity of the reaction increased with increasing alkalinity, but that the amount of thrombin ultimately formed decreased. Extraordinarily minute quantities of some of these venoms sufficed to produce a demonstrable activation of prothrombin. Thus, the fer de lance (*Bothrops atrox*) venom was active in a 1 : 25,000,000 dilution, and that of the Australian tiger snake (*Notechis scutatus*) was active in a 1 : 4,000,000 dilution.

" The thrombin formed was indistinguishable from that produced by the action of calcium + platelets on prothrombin. Like the latter type of thrombin, and unlike venoms which act directly on fibrinogen, thrombin formed from prothrombin by venom was inhibited by antithrombin.

" Every one of the 9 non-coagulant venoms in this series destroyed prothrombin ; and 5 of these destroyed fibrinogen as well. As is discussed in the text, there is reason to believe that these several properties of the venoms (coagulation and destruction of fibrinogen ; activation and destruction of prothrombin) depend on the proteolytic enzymes which they were found to contain.

" These observations lend further support to the thesis that, in the course of physiological coagulation, (*a*) calcium plus platelets (or tissue derivative) constitute an enzyme system which reacts with prothrombin to form thrombin, and which is thus analogous to trypsin and to several of the proteolytic venoms here discussed, and (*b*) the thrombin so formed is itself a proteolytic enzyme which, like papain and the majority of the coagulant and proteolytic snake venoms here studied, reacts with fibrinogen to form a fibrillar gel, fibrin."

H. H. S.

Higgins (Lionel) & Thorne (R. Thorne). **Epistaxis treated with Viper Venom.** [Memoranda.]—*Brit. Med. Jl.* 1936. Mar. 28. p. 640.

The authors record the case of a man of 63 years with a severe epistaxis. Repeated plugging of the nares and injections of so-called haemostatic serum, and of hazeline and adrenaline locally during 6 days proved ineffectual. There was a history of a severe bleeding on a previous occasion after tooth extraction and a brother was believed to be haemophilic. Viper venom [presumably *V. russelli*] was obtained and the nares plugged lightly with gauze soaked in it [strength not stated, but as it was obtained from the Wellcome Research Laboratory, it was probably 1 in 10,000, as is usual]. Haemorrhage ceased at once and had not recurred in the 3 weeks which had elapsed when the case was reported. *H. H. S.*

Hyatt (J. W.) & Buckland (F. E.). **A Case of Severe Epistaxis and Recovery following the Use of Daboia Venom as a Haemostatic.**—*Jl. Roy. Army Med. Corps.* 1937. Jan. Vol. 68. No. 1. pp. 54–55.

V. russelli venom has been used with good results in several cases of haemophilia, but the case recorded by the authors is of interest because of the venom being used for obstinate and prolonged haemorrhage following trauma ; there is no mention of any haemophilic taint.

The patient was a driver in the Royal Artillery with a history of epistaxis for six days following a blow with a cricket ball. Morphia, plugging the anterior nares with adrenalin gauze, the use of serum, had all proved ineffectual as haemostatics. His condition was serious when transported to hospital, a journey of 18 miles. Haemorrhage continued in spite of plugging of the posterior nares. Daboia venom, 1 in 10,000 dilution, was applied on an anterior plug, but bleeding continued behind it. Anterior and posterior plugging next morning with gauze soaked in the venom proved successful. By this time the pulse was 130 per minute, he was very blanched and respirations were

only 9 per minute. Convalescence was rapid and uninterrupted. The venom used was a preparation of the Kasauli Research Institute, a 1 in 10,000 dilution sterilized by filtration, and with 50 per cent. glycerin. Each 2 cc. ampoule contained 0·2 mgm. venom. Its coagulant activity had been retained for at least a year.

H. H. S.

Raimondi (Alejandro A.) & Sangiovanni (Adolfo). Tratamiento de las hemoptisis por el veneno de la *Vipera rusellii*. [**Daboia Venom in Haemoptysis.**]—*Prensa Méd. Argentina.* 1937. Jan. 6. Vol. 24. No. 1. pp. 42–46.

The strength of the solution utilized by the authors was 0·05 mgm. per cc., 1 cc. containing ten mouse-units (*i.e.*, 0·1 cc. was lethal for a mouse). They divided their patients into three groups, giving to one 0·25 cc., to the second 0·5 cc., and to the third 1·0 cc., and noted the coagulation and the bleeding time ¼, ½, 1, 2, 4 and 24 hours afterwards. The groups were very small, five in each of the second and third and two only in the first. Brief notes are recorded of nine of the patients. So far as general conclusions can be drawn on such a few cases, the authors found that the coagulant effect of the *V. russelli* venom was observed in a few minutes and increased up to two hours, beginning to return to normal after four hours; also that the intensity of the reaction was proportional to the quantity of venom injected, and, finally, that a dose of 0·05 mgm. could be repeated 4-hourly without danger. *H. H. S.*

Barratt (A.). **Haematemesis treated with Snake (Russell Viper) Venom by Mouth.** [Clinical Memoranda.]—*Brit. Med. Jl.* 1936. Nov. 28. p. 1083.

The patient was a thin, frail woman of 80 years who had suffered intermittently for the past 30 years from epigastric pain and vomiting; 22 years ago she "had a profuse haemoptysis" [? haematemesis]. In July of the present year (1936) her systolic blood pressure was 275 mm. On the 19th she vomited 1½–2 pints of blood, and this symptom continued in spite of rest in bed, and injection of morphine. In 24 hours she lost over 4 pints of blood. In view of her high blood pressure the haemorrhage was not at first regarded very seriously, but its persistence and amount were causing alarm and anxiety. The author had at hand some of Burroughs Wellcome & Co's "stypven," a Daboia snake venom product. He gave the contents of one phial of this by mouth. "There was no further haemoptysis" [again ? haematemesis]. A month later the blood pressure was 160/80 and 3½ months after the attack is the note "patient now fully recovered." Of course, haematemesis does cease spontaneously, particularly when an associated high blood pressure falls, but in this case the sequence was very prompt. A second point worthy of note is that no untoward symptoms arose ascribable to the action of absorbed venom. [Stypven is a preparation for local application of a strength of 0·1 mgm. dried venom per cc. On dilution it is said rapidly to lose its efficacy.] *H. H. S.*

HANCE (J. B.). **Experience with Russell's Viper Venom.**—*Indian Med. Gaz.* 1937. Feb. Vol. 72. No. 2. pp. 76–78.

Three cases are recorded and the venom was administered in three different ways. The first patient was a man of 48 years operated upon for infected tonsils by tonsillectomy. He stated that he was a "bleeder" and his coagulation time was found to be six minutes. Bleeding of an oozing type followed the operation and was not stopped by continued pressure or suture of the pillars. Local application of pledgets soaked in Daboia venom, 1 in 10,000, was followed at once by cessation of haemorrhage.

The second was a woman of 36 years operated upon for hysterectomy. Five hours later there had been copious haemorrhage and the patient's condition was desperate. 0·5 cc. of 1 in 100,000 solution of the venom was injected intravenously and repeated in 10 minutes.

The third was a man of 68 years having a cholecystectomy for gall-stones; three weeks prior to operation his coagulation time was 9 minutes 20 seconds and he owned to free bleeding from slight injuries in the past; by calcium therapy this was reduced to 6½ minutes and with haemoplastin to 6 minutes, but not less. Half an hour before operation 0·5 cc. of 1 in 100,000 dilution of the venom was injected intradermally, and at the start of operation the coagulation time was 4½ minutes. After his operation and on his return to bed the coagulation time was 5¾ minutes and another intradermal injection was given. There were no complications.

It is thus seen that the venom was given by direct local application in the first case, intravenously in the second, and intradermally in the third. Burroughs Wellcome & Co's preparation, Stypven, was used for all. *H. H. S.*

HANUT (Charles Joseph). Recherches préliminaires sur l'emploi des solutions diluées de venin de *Bothrops atrox* comme hémostatiques. [**Preliminary Study on the Employment of Dilute Bothrops Venom as an Haemostatic.**]—*C. R. Soc. Biol.* 1936. Vol. 123. No. 36. pp. 1232–1234.

The author's method of testing *in vivo* the coagulant powers of the venom *Bothrops atrox* is as follows: From a rabbit weighing about 2 kgm. is taken 4 cc. of carotid blood in 0·4 cc. of a mixture of sodium chloride and oxalate (NaCl 600 mgm., Na oxalate 1 gm. water (twice distilled) 100 cc.) Clear plasma is obtained by centrifuging and to 0·2 cc. is added 0·8 cc. physiological saline containing 1 gm. 50 mgm $CaCl_2$ to the litre and the time of coagulation noted. Next, 1 cc. of varying concentrations of *B. atrox* venom is injected into the jugular, and at intervals of 10, 30, 60 minutes, and then hourly, samples are taken and treated as detailed above. For example, after injection of a 1 in 500,000 dilution the oxalated plasma from the blood withdrawn coagulates 10–30 minutes later without any added calcium. On the other hand, 60 minutes or more after, the blood remains incoagulable even if calcium be added. The former is due to the action of the venom on the fibrinogen, and the secondary incoagulability is due to the defibrination.

It would seem that this secondary incoagulability would be an argument against the use of this venom as a haemostatic, but this

secondary effect was not observed if dilutions of 1 in 2,000,000 or more were used and even 1 in 5 to 10 million suffice and retain their coagulant properties, and moreover are non-toxic. *H. H. S.*

HANUT (Charles Joseph). Recherches préliminaires sur l'emploi, comme hémostatiques, des mélanges de venin de *Bothrops atrox* et de sérum antibothropique. [**On the Use of Mixtures of Bothrops Venom and Antivenene as Haemostatics.**]—*C. R. Soc. Biol.* 1936. Vol. 123. No. 36. pp. 1234–1235.

The author has found that in the rabbit the smallest amount of antivenene which will counteract the toxic effect of the venom of *Bothrops atrox* and that which will prevent its coagulant action *in vitro* are about the same ; secondly, that the employment of a serum more powerful than is needed to prevent the toxic action of the venom does not affect the coagulant action *in vivo*. Thus, a mixture is prepared of venom 1 in 70,000, 1 cc. per kgm. body weight, and varying amounts of antivenene, 20 minutes before injection into the jugular vein of the rabbit. With 0·006 cc. of antivenene the animal lived for 3–5 hours, the coagulant action was marked, the secondary phase of incoagulability might or might not occur (see above abstract) ; with 0·06 cc. the animal survived for 24 hours, the coagulant effect was obvious but no secondary incoagulability, and the same held good with 0·1 and 0·3 cc. of the antivenene. The smallest amount needed, therefore, to counteract the toxic effects was between 0·006 and 0·06 cc. The absence of the secondary phase was proved in the way described above. *H. H. S.*

REVIEWS AND NOTICES.

CHESTERMAN (Clement C.) [O.B.E., M.D.(Lond.), M.R.C.P., D.T.M. & H.(Camb.), etc.]. **Tropical Dispensary Handbook. An Aid to the Training and Practice of Native Medical Assistants and for the Guidance of all engaged in Medical Practice in Rural Dispensaries in the Tropics.**—Third Edition. Revised and Enlarged. pp. xv+ 299. With 19 plates. 1937. London: United Society for Christian Literature, 4 Bouverie Street, E.C.4. [7*s.* 6*d.*]

To quote the author's preface "This Handbook was originally compiled in 1928 from notes of lectures given to a class of African Medical Assistants." In this, the third edition, its scope has been extended in order to make it useful to workers elsewhere in the tropics. The subject matter is divided into four sections:—Medical diseases, tropical and others: Surgical diseases: A list of the more commonly used drugs, their action, dose, etc. and more important preparations: Laboratory notes.

As Dr. Andrew BALFOUR remarked in a Foreword to the first edition—"Within a comparatively small compass he [the author] has succeeded in bringing together a great deal of useful, accurate and up-to-date information on a variety of subjects . . . . There can be no doubt that this Handbook will prove of value to those for whom it is intended, although possibly it may be regarded as somewhat advanced for their immediate needs." That its value has now been proved is demonstrated by the issue of a third edition; that some of its contents are somewhat advanced is true. The method of presentation follows that adopted in TIDY's Synopsis of Medicine. TIDY presupposes a general knowledge of medicine on the part of his reader, Dr. Chesterman only some knowledge of anatomy and physiology, but it would seem doubtful if a Native Medical Assistant would *understand* the text of the Tropical Dispensary Handbook without having previously attended systematic lectures and clinical demonstrations. While all credit is due to the compiler of this volume there are a number of points which call for criticism, which could be easily corrected in a subsequent edition.

Phraseological abbreviation is made use of freely but sometimes with a sacrifice of clearness or truth, thus pernicious anaemia is covered by a single paragraph—"It is necessary only to mention this disease as a possible cause of anaemia, in adults only. It is severe anaemia caused by the lack of proper *formation* of red cells which may be *reduced* to under one million per mm^3. [reviewer's italics]. Probably this is due to a defect in gastric secretion. It results in the bone marrow sending out many immature cells into the circulation. Besides the symptoms of anaemia, there may be soreness of the tongue, and probably septic teeth. Nerve symptoms, paralysis, etc., may develop later."

There is evidence throughout of hurried preparation and lack of precision in writing—"Varicocoele [*sic*] is a condition *due* to enlarged and congested veins of the cord and *testis*." "Hydrocele is a *swelling of the membranes* (tunica vaginalis) surrounding the testis, with a clear fluid." "Epididymitis consists of inflammation of the epididymis or collecting tubules of the seminal fluid." "Boils. Signs and Symptoms. *They* may be *single*, or multiple, and may appear in crops." Nearly every page contains some similar example of careless phraseology.

Here and there important omissions occur ; thus in Tick Fever no mention is made of the pulmonary symptoms and irido-cyclitis in that disease. The geographical distribution of *Ternidens deminutus* is given as S. Africa only, etc.

Treatment, on the whole, is excellently described, but even greater detail might with advantage have been given in some cases.

H. S. Stannus.

Garniron (René). **Conservation des oeufs de quelques nématodes dans les fèces. Cas particulier d'Alger.** [Conservation of Nematode Eggs in Faeces with regard to Algerian Conditions.]—Thèse de Laboratoire de Parasitologie de la Faculté de Médecine d'Alger. Thèse No. 14. 160 pp. [Bibliography.] 1936. Algiers.

After ten main dedications this degree thesis passes on to a consideration of the literature dealing with the conditions suited to development of the eggs of hookworms, trichuris and ascaris. These are taken up under the headings of temperature, humidity, gases, culture media, urine and faeces, bacteria, acidity, chemicals, salt and sea water. After this the writer passes on to experiments of his own, cut short by the date on which the thesis had to be sent in. Development in cultures moistened with sea water was markedly slower than in fresh water, for when in the latter larvae were fully formed and active, in the former the outline of a larva had only just become visible. The practical points are that the sewers of Algiers discharge into the sea, that solid matter from them collects on the beach, and that sea water is used for road watering. Carriage of infection by air is accepted and the risk is pointed out of ascaris eggs being inhaled in dust from dried roads and elsewhere, or being eaten in sea dainties, among which are included oysters. *Clayton Lane.*

Schmidt (Hans) & Peter (F. M.). **Ergebnisse und Fortschritte der Antimontherapie.** [Results and Progress of Antimony Therapy.] —218 pp. With 8 figs. 1937. Leipzig : Georg Thieme, Verlag. [Bound M.17 ; Unbound M.15·50.]

Though the native sulphide of antimony was known to classical writers it was not till the later Middle Ages that the therapeutic possibilities of antimony were explored by the somewhat mythical Basil-Valentine and by Paracelsus and his followers. The chemotherapeutic use of antimony dates only from the present century when Plimmer and Thompson in 1907 showed that antimonyl tartrates possess trypanocidal powers. From this small beginning followed the discovery that in parasitic conditions as dissimilar as Leishmaniasis and Schistosomiasis the curative action of antimony is specific. At first the only antimony compounds used in chemotherapy were potassium and sodium antimonyl tartrates. Later " organic " compounds of quinquevalent antimony, with antimony joined directly to carbon became available, as a result of the work of Professor Hans Schmidt, who first described the process of diazo-synthesis. In this process, by the interaction of diazotized aniline and antimony trioxide, in the presence of alkali, phenylstibinic acid is produced. It is thus peculiarly suitable that Professor Schmidt, with the assistance of Dr. Peter should summarize our knowledge of the chemotherapeutic

action of antimony compounds. After a short introductory chapter, the various parasitic diseases encountered in human and veterinary medicine, in which antimony has been tested, are exhaustively discussed. The method of exposition is somewhat unusual, for in place of a continuous narrative, each page is split up into a series of rather disconnected paragraphs, headed by the name of an author with the title and reference to his paper. The book thus reads not unlike a bound volume of the *Tropical Diseases Bulletin* devoted entirely to the chemotherapy of antimony. While this arrangement is not without its advantages it is perhaps regrettable that the authors, with their encyclopaedic knowledge of antimony, have not seen their way to adopt a somewhat more critical attitude to the voluminous literature they have abstracted. Nevertheless, the volume will be of the greatest interest and value to all those who are interested in the young but vigorous science of chemotherapy. The reviewer pleads not guilty to having perpetrated a " Recent advances in tropical medicine."

G. M. Findlay.

Bono (Edmond). **Cysticercose cérébrale et syndromes épileptiformes.** [Cerebral Cysticercosis and Epileptiform Syndromes.]—Thèse du Laboratoire de Parasitologie de la Faculté de Médecine d'Alger. Thèse No. 9. 157 pp. [Bibliography.] 1936. Algiers.

After eleven dedications, the thesis itself deals with epilepsy caused by cerebral cysticercosis in terms of the ancient ban on the pig, measly or otherwise, from Moses onwards ; the parasite, which has been detected in 4 of 104,455 pigs killed in Algerian slaughter houses ; the pathological anatomy ; an abstract of 68 papers from the literature, with this *Bulletin* as the source of information in some ; the diagnosis, in which an important place is given to the amount of albumin in the cerebrospinal fluid drawn off by lumbar puncture, namely 0·4 to 0·75 [? per cent.] ; and the treatment, which it is held, can only be surgical. *Clayton Lane.*

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